Vol. 28 No. 140 August, 1953

DOES NOT CIRCULATE
UNIV. OF MICHIGAN
SEP 21 1953
MEDICAL LIBRARY

ARCHIVES OF DISEASE IN CHILDHOOD

INCORPORATING THE BRITISH JOURNAL OF CHILDREN'S DISEASES

EDITORS
P. R. EVANS and I. A. B. CATHIE

CONTENTS

	PAGE
Crossed Laterality; A Study in its Significance and Treatment in Ordinary School Life. ROBERT A. H. PEARCE	247
Accidental Poisoning in Childhood. J. O. CRAIG and M. S. FRASER	259
The Estimation of Blood Pressure in Childhood with Special Reference to the Choice of Standard Cuffs. H. SAINSBURY	268
Fourteen Cases of Idiopathic Myocarditis in Infants and Children. HOWARD WILLIAMS, R. N. O'REILLY and ALAN WILLIAMS	271
Left Auricular Enlargement in Endocardial Fibro-elastosis. J. L. FRAIN and W. S. MATHESON	284
Acute Isolated Myocarditis in Newborn Infants. J. M. DRENNAN	288
Thirty-eight Cases of Haemolytic Disease of the Newborn. Z. SHAKIR and J. GORDAVITCH	292
A Case of Congenital Diabetes. MARY B. S. WYLIE	297
Renal Thrombosis Complicating Pink Disease Cured by Nephrectomy. W. G. C. MILLS and T. K. OWEN	300
Haemorrhagic Infarction of the Kidney Treated by Nephrectomy. C. EMPLEY CLARK and J. D. PICKUP	302
Papular Urticaria. ARTHUR ROOK and W. FRAIN-BELL	304
Foetal Vaccinia. A. M. MACDONALD and P. MACARTHUR	311
E.E.G. Findings in 100 Cases of Severe Enuresis. E. C. TURTON and A. [illegible] SHAW	316
A Case of Congenital Hemihypertrophy Showing Variations in Bone Age and Development. F. STEPHEN CARTER and G. C. DUCKERAY	321
Enterogenous Cyst of the Mediastinum. T. A. SALE	325
The Treatment of Ascaris Infection with Veterdon. J. H. P. JONES and [illegible]	329
A History of Infant Feeding: Part III. Eighteenth and Nineteenth Century Practice. IAN G. WICKES	332
Book Reviews	341

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION (6 NUMBERS £3 3s. 0d.) U.S.A. $11.00 SINGLE NUMBER 12s. 6d.

EDITORIAL COMMITTEE

J. J. Mason Brown
John Craig
R. W. B. Ellis
Wilfrid Gaisford
R. S. Illingworth
W. W. Payne
J. M. Smellie
K. H. Tallerman
A. G. Watkins
R. B. Zachary

President of The British Paediatric Association
Editor, *British Medical Journal*
Appointed by The British Paediatric Association and The British Medical Association

GENERAL ADVISORY BOARD

F. M. B. Allen (Belfast).
H. T. Ashby (Manchester).
Cecile H. D. Asher (London).
Alan Brown (Toronto, Canada).
J. J. Mason Brown (Edinburgh).
N. B. Capon (Liverpool).
Robert Cruickshank (London).
Helen Deem (Dunedin, New Zealand).
Lorimer Dods (Sydney, Australia).
Harry Ebbs (Toronto, Canada).
William Emdin (Cape Town, South Africa).
Jean Mackintosh (Birmingham).
Alan Ross (Montreal, Canada).
H. J. Seddon (London).
Eric Sims (North Adelaide, Australia).
H. L. Wallace (Durban, South Africa).
Howard Williams (Melbourne Australia).

NOTICE TO CONTRIBUTORS

Papers for publication should be sent to Dr. I. A. B. Cathie, The Hospital for Sick Children, Great Ormond Street, London, W.C.1.

Submission of a paper for publication will be held to imply that it contains original work which has not been previously published. Permission to republish must be obtained from the Editors.

Papers should be as concise as possible and illustrations kept to the minimum. Manuscripts should be typewritten top copies in double spacing. They should have been carefully revised, and alterations in proof, apart from printers' errors, are not permissible.

Photographs and photomicrographs should be submitted unmounted. Drawings and diagrams should be boldly drawn in black ink on stout white paper. Any necessary lettering may be lightly inserted in pencil.

Overseas contributors should nominate somebody resident in Great Britain willing to correct their proofs and deal with the subject of reprints.

Current numbers of the *Archives of Disease in Childhood* should be consulted for information concerning standard abbreviations, etc. In references to papers in the text the year of publication in parenthesis should follow the author's name. References at the end of the text should be in alphabetical order of authors' names, and titles of journals should be abbreviated according to the *World List of Scientific Periodicals*. Book titles should be followed by the place of publication.

Failure to observe the above directions may result in the return of typescripts to authors for correction, with consequent delay in publication.

Twenty-five reprints are supplied free. Further reprints must be ordered when returning proofs.

Subscription. £3 3s. 0d. per annum, post free.

Applications for advertising space should be made to the Advertisement Manager, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

CROSSED LATERALITY

A STUDY IN ITS SIGNIFICANCE AND TREATMENT IN ORDINARY SCHOOL LIFE

BY

ROBERT A. H. PEARCE

From the China Inland Mission School, Kuling

(RECEIVED FOR PUBLICATION JANUARY 20, 1953)

All paired muscle systems are represented in the brain by paired controlling centres. Dominance, or leading control of the function, may be entirely left-sided, in which case the organs controlled are dominant on the right side, or entirely right-sided. If some centres are on the left and some on the right side of the brain, the condition is called crossed laterality.

The dominance may be fixed, and diagnostic methods give no variation in results. In some children there is less fixity, one or the opposite centre taking control according to whim or circumstance.

These investigations were provoked by the observation of educational problems arising in a school of 150 to 200 children of both sexes between the ages of 6 and 16. The observations and investigations were carried on over a period of four years. The examiner knew all the children intimately, and lived among them continually. Thorough physical examinations were made at intervals of approximately nine months. Intelligence was measured and re-measured, using Terman and Merrill's tests, and Raven's progressive matrices. The teaching staff of the school used to meet regularly and frequently for discussion of the progress, educational problems and conduct of each child. In the capacity of School Medical Officer I attended all such meetings. There were unrestricted opportunities for investigation of these problems.

During the work report meetings it was noticed that some 40% of the children, at one time or another, presented some difficulty or failure in educational attainment. A further search revealed that 70% of these children had some type of crossed laterality. Viewed from another aspect it was known that 47% of the children in the school had crossed laterality, and of these 85% were in the group who experienced difficulties in school work.

The work here recorded was planned to discover: (1) Symptoms arising because of crossed laterality; (2) the effect of these symptoms on education; (3) the mechanism whereby these symptoms are produced; (4) why some cases of crossed laterality were asymptomatic; and (5) effective means whereby the handicap of crossed laterality might be overcome.

The Symptoms

Reversal of units in a series was the most prominent and basic phenomenon observed. This was found in any of the 'three R's' at any age. The child was never conscious of the error until it had been made. The symptoms to be described are not observed on every possible occasion. In different children they are present with varying frequency and persistence, depending upon the nature and the fixity of the irregularity, and upon what compensations the child has developed. Other factors which influence the appearance of symptoms are emotional tension at the time of examination; the type of teaching which the child has experienced, and the associated mental stress; the intelligence; and the speed with which puberty is being attained. No child will show all the symptoms observed, but each type of 'crossing' is associated with certain sets of symptoms. These symptoms do not occur in children without irregular dominance. Any child may make a mistake, and in the course of ordinary probability any particular mistake may be made. Those children who have these forms of irregular dominance show these symptoms frequently and persistently. Further, they find difficulty in learning to correct the mistakes, for the error occurs unconsciously.

It is not at all uncommon for children who are just learning to write to reverse letters, as b for d, or vice versa. Normal children learn the correct form quickly and without difficulty. Children with

irregular dominance are slow to make the correction, not readily appreciating the error. They have a marked tendency to repeat the error unconsciously. In older children the error may appear so that they seem to make careless mistakes in compositions and arithmetic. One can look upon a letter or figure as a diagram. More complicated diagrams have been prepared, and reversal of units of these may frequently be found when these are reproduced by children with irregular dominance. For example, this diagram (from Terman and Merrill's tests Form L 9 years) copied from visual memory may be reproduced with the corner units reversed thus:

When reading, reversal of the letters of a word may make something unpronounceable and meaningless, or occasionally a word that does not fit the sense. In the former instance, reading will be slow, and the child appears to stumble at small words. In the latter case the wrong word is read, delaying the perception of content, or if read aloud, the child is embarrassed and appears to others to be stupid. As an example, the child reading 'He saw a plum' may perceive and read 'He was a plum'. A similar fault is found in arithmetic, for the child reads or copies the figures of a problem in reverse, as 54 for 45 or 729 for 792.

Perception by hearing leads to reversal symptoms less frequently than if perception is by vision, for the opportunity is less. I have known it to occur when a child looks for a hymn that has been announced during a service of worship if he cannot see the hymn board.

It is characteristic of children learning to write, who have crossed dominance of eye and hand, that if the accepted normal standards of writing—position of person or paper and pencil—are rigidly enforced, the resulting script is poor. If the children are left alone to write as they please the script may still be poor, but they will twist the paper or the head. The children do not know why they do this, but all affirm that it is easier for them to write in this 'awkward way', and a diagnosis of 'poor muscular control' is frequent.

Children who use a left foot dominantly show no closely related symptom, but may provoke a laugh from their fellows who consider the foot work strange and awkward. But if the ability to kick well with a left foot wins for such a child acceptance as having a special ability, he will avoid the emotional upset commonly seen to follow the symptoms of irregular dominance.

Children having complete left dominance show some of these symptoms, but with characteristic differences. Reversal mistakes in reading occur, but not in listening. Some prefer to write along lines that are oblique to the body. The use of the writing left hand above the line of script is only a means by which what has been written may be seen, the hand not then obstructing the view. Not all children using the left hand are completely left-handed; some have crossed laterality, and show the symptoms noted above.

Attempts to force the child to use dominantly a function which is not naturally dominant will cause symptoms to arise from the induced crossing, and also certain other evidences of cerebral turmoil. Symptoms arising thus are minimal when the crossing is not fixed, and when intelligence is high. The most widely known symptom resulting from attempts to change dominance is deranged speech. This can vary from complete aphasia to varying degrees of stammering. Other signs of nervous upset are also seen—not in themselves pathognomonic—such as enuresis and encopresis.

The emotional upsets that develop because of these symptoms are not isolated events but grow as the errors recur. The form which they take will depend upon factors such as age, development, speed of growth and intelligence. The following story is typical: The little child learning to write has a very poor hand, and the teacher finds that efforts to bring improvement meet with little success. Mistakes in reading recur so persistently that the teacher naturally begins to suspect that the child's mental capacity is not equal to the appointed tasks. Should he read silently, the content is gained too slowly; should he read aloud, errors are made over small words, and he becomes a source of merriment to his fellows. In arithmetic the persistent mistakes are labelled 'careless'. In consequence we find the child is frequently embarrassed in his class, and begins to echo his teacher's suspicion that he is mentally slow. He says, 'The harder I work, the worse I do.' It is easy, even reasonable, to cease to try hard and to drop into lazy habits. These children are difficult and often exasperating. No child of high intelligence fails without suffering, for he is conscious of ability and rebels against the suggestion that he is 'dumb'. He either becomes lazy and difficult or embarrassingly nervous, failing to keep pace with others, in spite of what appears to be tremendous effort.

How deeply this emotional trauma affects the child depends upon inherited physical factors and

upon intellectual capacity as well as upon the environment. The emotional conditions observed can be classified under certain factors thus:—

High Intelligence and Quick Development. If the irregularity is not fixed there is little of note except that the child learns more slowly than a similar child without the handicap.

If the irregularity is fixed, natural compensations develop with speed depending on the type of crossing and the intelligence. These children respond to sympathetic, helpful handling and symptoms are overcome. In cases where there has been other educational lack, or where there has not been good teaching, some symptoms will persist. The lack of progress will be covered by indifference leading sometimes to actual laziness.

High Intelligence and Slower Development. Whatever the fixity of the irregularity, these children are diffident. Natural compensations occur more slowly, and the child is constantly finding frustration. These children do not make progress as quickly as one might expect from knowledge of the I.Q.

Average (and Lower) Intelligence, with Quick Development. Symptoms are definite. Compensations are only slowly attained. Persistent mistakes stimulate a rebellious attitude towards the teacher, and methods of escape are planned and effected.

Average (and Lower) Intelligence with Slow Development. Symptoms are definite. Compensations are slowly attained. These children tend to be vindictive. The frequent mistakes and slowness to learn will be blamed upon their teachers.

Emotional disturbance is probably of greater importance ultimately than educational backwardness. When a child has failed to attain an adequate standard of reading and writing he will find his way into some gainful occupation which is not dependant upon these abilities. If he has grown up with feelings of frustration, inferiority and diffidence, these will prove ever present trials in any walk of life.

Diagnosis of Ear, Eye, Hand and Foot Dominance

It is reasonable to speak of dominance of one of a pair of these functions only if each of the organs concerned is practically normal. The ordinary variations between the eyes, due to differences of refraction, do not determine dominance. The following methods have been found to give consistent results. When seeking to determine dominance it is essential that the child be absolutely at ease, happy and generally interested and yet ignorant of the object of the test. It is a good plan, therefore, to space out the tests at different times in the course of a physical examination, and also to use a variety of tests.

Ear. During examination of the ears for hearing acuity the child is made to stand in front of the table upon which rests a watch on a cushion. He is asked if he can hear it. The watch is then covered by a cloth, or placed in a box, and the question repeated. If the child is not able to hear the watch, he is told to get closer to it, and still closer until he can. It will be observed that as the child bends or approaches the watch, he will bring either the right or the left ear nearest. This is the dominant ear. This test must be varied in form from time to time and from child to child.

Eye. Many tests have been described for the determination of eye dominance. Some have proved unreliable in small children because of difficulty in gaining their cooperation. The following tests and simple variations have been found reliable. A small bright object on the far side of the room is observed by the child through a small circular hole about $\frac{1}{2}$ in. in diameter in a card held at arm's length. The examiner stands behind the child and observes the line object-hole-eye. This eye will probably be the dominant eye. While still in that position, the other eye is shaded and the child asked if he can still see the object. If the original line has been noted correctly by the examiner he will answer in the affirmative. The presumed dominant eye is now shaded. The child will say that he does not see the object, and will move the card until the other eye takes up the line. There is more difficulty in lining up the non-dominant eye. The card will be moved up and down and round about until it is in position, an action quite distinct from the quick way in which the dominant eye is lined up. This test is very reliable, but too difficult for small children.

The following test I have found acceptable to a small child; it gives satisfactorily consistent results and can be modified almost indefinitely according to circumstances. On the hillside opposite to my consulting room there was a wooden shack which had three windows of different sizes. The child was given a cardboard tube, told to pretend that it was a telescope and to look at the 'large-sized window, the middle-sized window and the smallest window' to see if any of the bears could be seen. The child uses the dominant eye. A kaleidoscope, a toy telescope and such playthings can be used effectively.

During a test for visual acuity the child is given a small refraction mirror with a central hole. He is told to use this looking from the black side through

the small hole at the lower letters on the eye chart to see if they appear blacker. He will use the dominant eye, and in most cases make no movement to use the other, indicating that his thoughts are on the letters rather than the eye. The result is therefore the more likely to be reliable.

Hand. If a small child is given a pile of blocks and is told to build a tower, the highest blocks, whether the pile is of single or of many columns, will be placed with the dominant hand, for that can be used more delicately and with better control. Older children, able to write, will use either a dominant right hand naturally, or a right hand which has been 'changed', or a dominant left hand. The child then takes the pencil in the other hand and endeavours to write. The dominant right-handed child holds the pencil awkwardly and does very poor script or none at all. The 'changed' child takes the pencil with the left hand, holds it easily and makes a presentable script. The true left-handed child finds the use of the right hand as difficult as his right-handed fellow does the left hand. The dominance of eye and hand together may be shown if a child is asked to thread a needle. He will observe the eye of the needle with the dominant eye, and may even close the other eye. He will hold the thread in the dominant hand, for this hand will have to make fine movements, and the needle in the non-dominant hand, for no movement is required at all.

Leg. When the little child has built his tower of blocks he is given a small wooden ball, which is placed on the floor 6 or 10 feet away. He is told to kick the ball so that it knocks the tower down. It is probable that he will have to make more than one attempt. Accurate aim when kicking is obtained only by using the dominant leg. In older children this may have become apparent already for the child is known to be a useful left wing in football. Older children have been tested in the following manner. Standing on the far side of the room from the examiner, they are told to kick back to him a ball he rolls to them. A child with a dominant right foot will do this with the right foot. The ball is rolled again, but this time to the right of the child. He will still return it with the right foot. The ball is then rolled again to the left of the child, and the child will turn so that he will kick the ball back again with the right foot. A child whose left leg is dominant does just the reverse at these different stages.

Balance has been used to determine leg dominance, for the dominant leg or foot is used to restore position to the body when the balance has been upset. This is best observed in the child's play. Any test designed to upset the child's balance may frighten him if unexpected and so spoil 'rapport' between examiner and child. But if the child be warned, he will not act naturally or unconsciously, and the value of the observation becomes questionable.

As has been noted, observation in work and play can be of great value, and is almost the only reliable way of tackling the problem in very young children. Some acts, such as the 'high jump' and digging, use a number of organs, and can be used in confirmation of the results obtained by the specific tests.

Equivocal results indicate that dominance in one of a pair is not fixed. If modifications of the test are made on different occasions it will be seen whether there is real lack of dominance, or whether the equivocal result is due to lack of understanding on the part of the child. The lack of complete dominance is revealed by the use of one of the organs concerned, but a readiness to use the other if that be more convenient. For example, one ear will be used, but if the child cannot hear, he may turn and use the other; one eye will be used, and then the other; one foot may be used to kick the ball back to the examiner, but when the ball rolls nearer the other foot, this will be used as easily as the first. Such results are of importance, for they have a bearing upon prognosis of treatment.

Notation

The following notation has been found convenient. The capital letter R and L indicate dominant function, as right or left (not cerebral centre). When either of the paired organs may be used satisfactorily, neither being dominant but used according to the subject's convenience, small letters are used, r and l. But in these instances they will of necessity be in pairs, rl or lr. When the dominance is definitely on one side, but there is ability on the other, it is indicated thus, Rl or Lr. The organs described are recorded in the order, ear, eye, hand and foot. If, for some reason, the dominance of one of a certain pair cannot be determined, as for example if the subject has a blind eye, the space in the series is noted by a full-stop. When the position of the centre is not known its place is indicated by O. If the type of dominance is irrelevant to the argument, this function is indicated by the oblique line /. The position of the speech centre is indicated by the use of R or L in brackets (R) or (L). This naturally refers not to the observed function but to the actual cerebral centre.

For example, R R R R indicates that the subject's ear, eye, hand and foot, are dominant on the right

side, the cerebral centre being on the left. L L R R indicates that the subject's ear and eye are dominant on the left side, but that the hand and foot are dominant on the right. R L Rl L indicates that though the right ear, left eye and left foot are dominant, the right hand shows more skill than the left, but the left also has ability. L R (L) R L indicates that dominant function of ear and foot are on the left, and of eye and hand on the right. The speech centre is deduced by experiment to be on the left side of the brain.

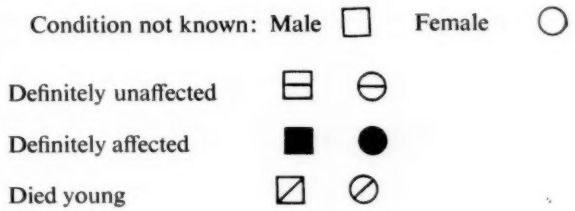
Aetiology

A clue has been found to the development of crossed laterality from a study of family histories, The children in this series belonged to 70 families. All the cases of irregular dominance were found in 57 of these families. Fresh cases of crossed laterality were found among other brothers and sisters of these families, not pupils of the school. Those children who showed equivocal findings all had sibs with definite irregular crossing, and therefore showed the condition in the family tree. Similarly, an isolated left ear dominance was found only in those families where there were other types of crossed dominance.

Complete and accurate family histories are rarely obtainable, for diagnosis in an adult may be difficult or, if absent, impossible. Occasionally one can learn of relatives who were definitely left handed, or were known to have left dominance of eye or foot. Again, one hears of relatives in these families who were known to have shown symptoms, particularly bad writing, bad spelling, stuttering, or of having been changed from right to left handedness.

The condition may arise spontaneously in one of uni-ovular twins, one having complete right and the other completely left dominance. Most commonly it is found that one or other or both of the parents have irregular or left dominance. Among the offspring complete left and complete right dominance or any type of crossing occurs. Occasionally I have found two or three children in a family with definite irregularities but with no relative known to have anything but the usual right dominance. I have also noted apparently normal parents who have brothers or sisters affected. These latter two observations raise the possibility of the transference of a recessive factor, but such instances are the exception. An obvious family history is the rule.

The following family trees are typical of those collected. Incompleteness is largely due to the relatives being scattered over four continents, and therefore beyond examination, and sometimes unknown to the parent questioned. These symbols have been used:



The letters by the symbols refer to description in the legends of the individuals marked.

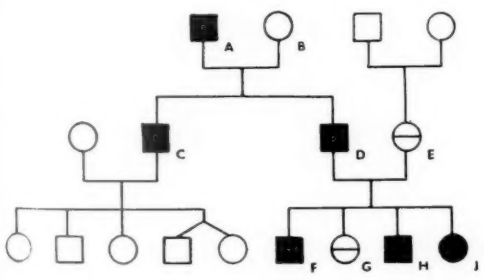
All subjects known to show any left-sided dominance, complete or incomplete, are regarded as 'affected' in these pedigrees, and in this section of the discussion.

These five histories illustrate the conclusions regarding inheritance which have been confirmed by similar histories of other families. Persons examined are indicated.

Families 1 and 2. Show inheritance through three generations.

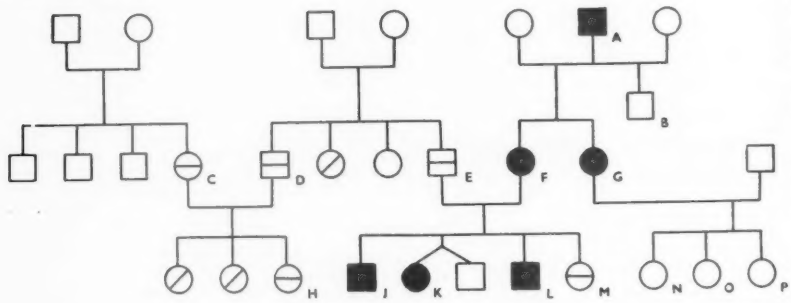
Family 3. Shows persistence of genetic factor, in spite of an apparently successful change of mother from right to

Family 1



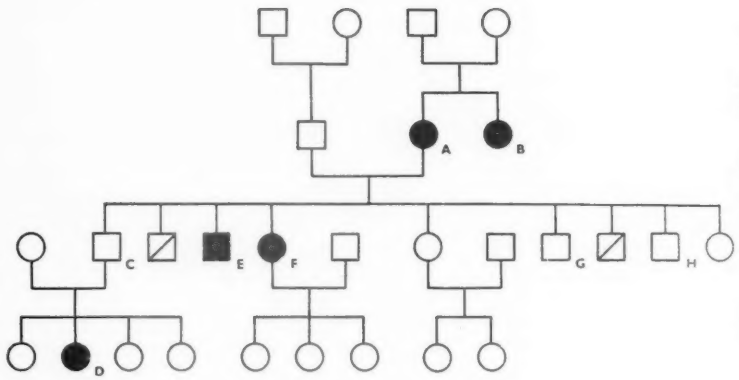
A. Known to use left hand and foot, but having right hand ability.
B. Known to use right hand and foot.
C. As A.
D. L L lr L. University graduate.
E. R R R R. Knows of no symptoms in family.
F. rl R R R. No symptoms.
G. R R R R. No symptoms: clever.
H. lr L R R age 6: early schooling very handicapped by symptoms.
J. L L L L age 4. Has had no schooling.
D, E, F, G, H and J are the only individuals known and examined.

Family 2



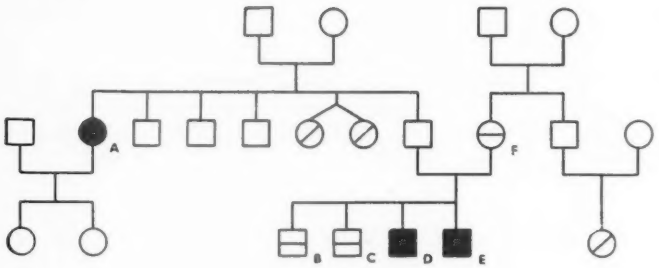
A. Left handed.
B. Thought to be right handed.
C. D. E. Completely right, without symptoms.
F. L L L L.
G. Attempt was made to change dominance—failed entirely.
H. Completely right, no symptoms.
J. Lr R R R. Average ability, very little trouble except enuresis.
K. rl R R rl. Average ability; no symptoms.
L. L L R R. Stuttered as a child, fair ability, handicapped by bad spelling.
M. R R R R. Poor ability but no symptoms.
N.O.P. No known symptoms, thought to be right handed. Not examined.
C, D, E, F, H, J, K, L, M are the only persons known and examined.

Family 3



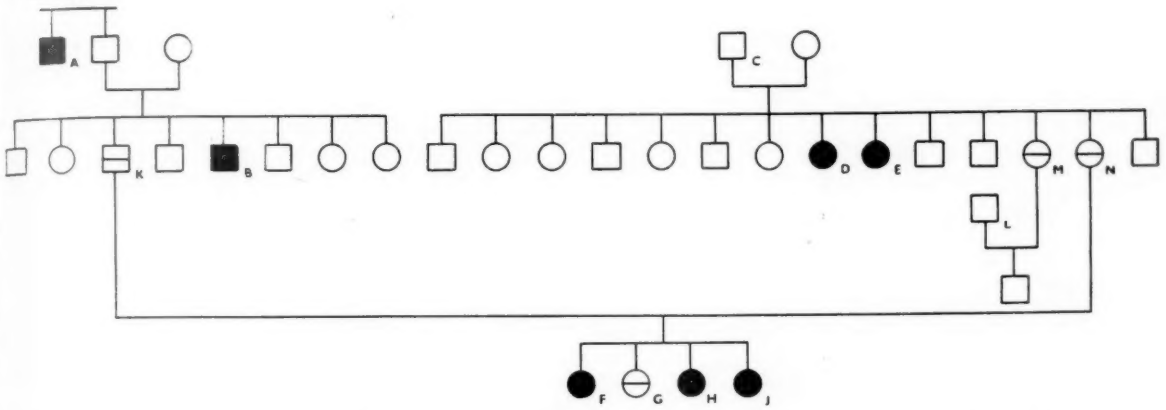
A. Changed from left to right hand for writing.
B. Left handed.
C. Right handed, no known symptoms. Very clever.
D. Left handed aged 3.
E. L R L R. Intelligent, but very poor writing.
F. Left handed. Family not known.
G. School work slow and poor. Blinks continually. Right handed.
H. Suffers with a nervous tic.
E is the only individual known and examined.

Family 4



A. Left handed.
B. R R R R.
C. R R R R. High intelligence.
D. L R R R.
E. R L R R. Poor average I.Q. not yet at school.
F. R R R R.
A, C, D, E, F all known and examined. History obtained through F who was not very familiar with her husband's family.

Family 5.



Family history obtained from K, L, M and N, who were all unaffected.
F.G.H. known and examined, J. abroad, age 4.
A. A left-handed bowler.
B. Left handed.
C. Able to read well, but would never read aloud.
D. Left hand, changed to right and became bad in reading and writing. Stuttered.
E. Backward in spelling and reading with symptoms of emotional upset through schooling.
F. L L Lr Lr. Average intelligence, backward at school because of very troublesome reversals.
G. R R R R. No symptoms.
H. L R R R. No symptoms under ordinary conditions.
J. Known to be left handed. Not examined because of being abroad.

left handedness. Also illustrated the possibility of a child inheriting the condition through a parent not known to have symptoms, and possibly without the condition.

Family 4. Shows inheritance through an apparently normal father, in whose family there is left handedness.

Family 5. Left handedness is recorded in the families of both parents (in the case of one, with very severe symptoms), though each parent is apparently normal. The mother, N., had lost the sight of the right eye through an accident when aged 18 months.

Natural Compensations for the Symptoms

How frequently the symptoms of crossed laterality occur depends on the extent to which compensatory methods are developed. The presence and significance of these are unknown to the child in the majority of cases. They arise unconsciously, and are most developed in children with high intelligence and of fixed irregularity. Correct perception is obtained by multiplying the stimuli received. The lesser the child's intelligence, the slower he will be able to compensate in this way.

When the ear is used a smooth, soft monotone is a single stimulus. If rhythm or emphasis be added to the sound, the memory of music is also stimulated. The louder the sound heard, the more likely it is that both ears will be used, and not the dominant ear alone.

The child looking steadfastly at a design he has to reproduce from memory will sometimes be observed to move a finger as though following the pattern as he will draw it. This addition of kinaesthetic memory ensures correct perception. Ocular perception is sometimes corrected at a later stage. When the child perceives that what he has read does not make sense he will re-read correctly. This depends entirely on his mental ability. Slower children go to the stage of transferring the perception to speech. Then, having heard what they have said, the need to correct is known and effected. Just as loud sounds make incorrect perception unlikely, so large visual images are more accurately remembered.

A still different approach has been seen among those children whose irregular dominance leads to incoordination of hand and eye. When writing they turn the paper so that the line of writing is at an angle to the body. They find this easier and their efforts more acceptable.

The Course of Crossed Laterality Uninfluenced by Treatment

Crossed laterality has been brought to notice in recent years, not only by careful observation, but because a greater opportunity for the development of symptoms as formal education has become more general. Persons engaged in outdoor or manual occupation are not subjected to the same mental activities as those engaged in more intellectual tasks, and do not show these symptoms. If the early

schooling has been adequate the intelligent child unconsciously gains compensation for his handicap, and is almost without symptoms.

I have found no evidence that real change of cerebral dominance ever occurs. If the dominant one of a pair of cerebral centres is destroyed before the age of 5 or 6, the other will gradually gain complete control of the function. At a later age full function is never attained. When one of the organs becomes useless a similar course will be followed. In neither of these instances is the basic inherited pattern altered, nor are the genetic potentialities of the individual changed.

Varieties of Crossed Dominance Found in this Series

Groups I and II. L R R R, 16·0%; R L L L 0·6%. These are almost without symptom or handicap in ordinary school life. Under artificial condition reversal can be demonstrated from reception by hearing to expression by speech or writing.

Groups III and IV. L L R R, 10·6%; R R L L 0·6%. The most serious symptoms occur in these groups.

Groups V and VI. L R L R, 1·2%; R L R L, none found. Reversal symptoms occur in speech and writing, but corrective mechanisms readily develop.

Groups VII and VIII. L L R L, 1·2%; R R L R, none found. Reversal symptoms occur in speech and writing, but corrective mechanisms readily develop.

Groups IX and X. R L R R, 14·6%; L R L L, 0·6%. Serious symptoms occur as in groups III and IV.

Groups XI and XII. R L L R, none found; L R R L, 0·6%. Symptoms as in groups I and II.

A potential handicap was present therefore in nearly 28% of children in this series.

Complete left dominance was present in 4% and complete right dominance in 49·3% of the children seen. The sex distribution was equally divided, both among the children with crossed lateral anatomy and the remaining children. There was a very slight, probably insignificant preponderance of males among those showing symptoms that could be related to this condition.

When the intelligence quotient is 120 or higher evidence of crossed dominance is readily masked by the child's unconscious development of compensatory mechanisms.

Experimental Investigation

Although unconscious reversals occur spontaneously in ordinary school life, they can also be provoked artificially. This was observed while making intelligence tests with the material prepared by Terman and Merrill. In the course of repetition of a series of figures it was found that a child with irregular dominance might reproduce all the digits but reverse the position of two. This error was not perceived by the child, who appeared satisfied that he had done what had been required. Because of errors of this kind a serious number of months of mental age might be lost, vitiating the quotient. By accepting the series as correct, even though two units were reversed, a quotient more in keeping with the findings of other non-verbal tests was reached.

Many series of figures and letters were prepared for presentation to the child in these experiments. Care was taken that each should be a single stimulus. Thus, letters like b and d were not placed together in a series, nor as terminal letters in consecutive groups; letters in alphabetical sequence, and those occurring together in spelling frequently, as g and h, or t and h, were omitted. Letters were not grouped so that any word or well known acronym could be assimilated, as **W H Y C**, or **U N O X**, or **S T M W**; all vowels were omitted because words or syllables might be formed. Letters which might be confused with other letters through similarity of sound were not used, as j and k. The figure series were constructed so that there should be no sequence or progression which might have been appreciated by a bright child, as 2 8 3 4 7, or 1 2 4 8, or 2 3 7 8, or 4 1 8 5, and so on. Throughout the experiments no child was given the same series twice. Fourteen distinct series of letters and figures were prepared for each child, and if repetition were subsequently required another series would be constructed.

The ability to reproduce a series depends upon the mental age of the child. Three groups of three were first presented; then three groups of five; three groups of six; three groups of seven; and three groups of nine. With figures it is known that a mental age of 3 repeats three figures, of 4½ four figures, of 7 five figures, of 10 six figures; series of eight and nine figures are repeated by those having a high adult standard of intelligence.

Letter series of similar length could be repeated at about the same intelligence level. Reversal of units occurred unconsciously with those having irregular dominance, even from the shorter series, but as soon as a series above the mental age level was reached, this type of error was replaced by complete confusion of the units repeated, in kind, number and order. The child became conscious of error, and no useful purpose was served by proceeding with the tests at these higher levels, for it

caused the child to become embarrassed and spoiled *rapport*.

The method of presentation was carefully planned so that the child met a single stimulus. At a later stage in the tests two single stimuli were simultaneously applied. When hearing was to be used, the series was spoken to the child by the examiner in a soft regular monotone, at a rate approximating to two units a second. A simple apparatus was constructed so that the child might view the series for a similar length of time, after which it became hidden. The letters were in block capitals, and both letters and figures of a size corresponding to 6/6 vision at 3 feet. Similar series were prepared so that they might be presented to the child vertically.

Expression was made to be a single effort. When writing the child was told to write immediately and not to repeat to himself, either before or while writing, the series. This was not always easy for some children because of habits they had formed. It was observation of this difficulty and its effects which suggested the combination of expression; thus, the child would write what he had seen or heard, and then repeat it by speech without reading what had been written. And, alternatively, he would repeat what he had perceived, and then write it.

These tests are time consuming, and the child easily becomes fatigued. It was found best to keep even the most intelligent no longer than 20 minutes at any one time and to complete the tests on subsequent days.

The findings are summarized in the table on page 256.

If the child's eyes are watched as he reads—a mirror is placed in the plane of the book and the observer stands behind the child—they will be seen to move in tiny jerks from side to side. If the right eye is dominant the eyes jerk towards the right; if the left is dominant, although the eyes are still moved towards the right, sudden movements in the opposite direction occur simultaneously with reversal of what is seen, or a stumbling in the reading. When presented with a picture of a number of objects, none being a principal feature, the child who is right eyed will enumerate the objects from left to right, and the left-eyed child will do the reverse. The movement of the eyes may be known subjectively when travelling at speed in a train. The right-eyed traveller, facing the way he is going, reads notices or station names more easily if he looks over his right shoulder than similar notices seen as he looks over the left. When he sits with his back to the engine the opposite is true. But, if the traveller is left-eyed, all these observations are reversed. In the foremention experiments it was found that, while horizontal presentation of a series to the eye resulted in reversals appearing, vertical presentation did not do so. Children with the cerebral pattern / L L/, and /L R/ find that they can write better and more comfortably with the book on a slant. The hand moves of necessity from left to right, but the eyes do not follow this direction naturally. By using an oblique path the eye can maintain control over the hand more easily. When a child writes a line six inches long, parallel to the line of his shoulders and eighteen inches distant, the eyes must sweep through a horizontal angle of 20°. If the book is turned through an angle of 60° the horizontal sweep of the eyes is through 8°, and the vertical sweep through 16°. If now the plane of the book is depressed from the child through 45° the vertical sweep required of the eyes is now $10\frac{1}{2}$°.

The Mechanism of Reversal Symptoms as Deduced from Experimental Findings and Observed Natural Compensations

Dominance of a cerebral centre ensures that the function of the corresponding muscle is delicate and accurate. In the ear the tensor tympani controls the sensitivity of the drum to the pitch of the sound sought. Each ear may be completely sensitive throughout the whole range of audible sounds, but the child prefers to use one ear when listening intently and so, presumably, the impression is more fixed on that side of the brain. Observations of eye movements show the method by which reversal occurs. Accuracy of vision is determined by use of the ciliary muscles, and so there is preferential use of a single eye when observation is made through a small aperture. Because of the optic decussation, visual perception is equal on each side of the brain. Similar delicacy of control is attained in both hand and leg or foot movements through a dominating cerebral centre. This is noticeable when a child builds a high tower of blocks, and when he attempts to use the non-dominant hand for writing.

The reversal symptom arises when what has been perceived is expressed through the medium of a dominant cerebral centre which is on the opposite side of the brain from the dominant centre of perception, as is shown in Experiment 1. Visual perception is not reversed in this way, for both sides of the brain have been equally stimulated. When the eyes are required to observe and reproduce a series in a direction opposite to the natural movement, irregular movement of the eyes will result in inaccurate perception, and consequently in inaccurate expression. This is demonstrated in Experiments 3 and 4.

Speech is controlled from two cerebral centres.

Experiment No.	Method of Reception	Method of Expression	Dominance Patterns showing Reversal Symptoms	Types of Crossing according to Groups (page 254)
1	Hearing	Writing	Right ear and left hand dominance and vice versa	I, II, III, IV, VII, XII
2	Hearing	Speech	Found sometimes when ear and hand dominance were opposite, and also when ear and eye dominance were crossed, even though ear and hand dominance were in agreement. This suggests that in such cases the speech centre is situated in the cerebral hemisphere corresponding to eye dominance rather than in that related to the dominant hand	I, II, III, IV, V, IX, X, XII
3	Sight	Writing	With left eye dominance irrespective of hand dominance	II, III, VII, IX
4	Sight (horiz.)	Speech	With left eye dominance irrespective of hand dominance	II, III, VII, IX
5	Sight (vert.)	Writing	None	
6	Sight (vert.)	Speech	None	
7	Hearing and sight (horiz.)	Writing	None	
8	Hearing and sight (horiz.)	Speech	None	
9	Hearing	Writing then by speech	Reversals occur at the first as in Experiments 1, 2, 3, and 4	
10	Hearing	Speech then by writing		
11	Sight	Writing then by speech	If reversals occur at the first stage they are repeated	
12	Sight	Speech then by writing		
13	Hearing and sight (vert.)	Writing	None	
14	Hearing and sight (vert.)	Speech	None	

This is to be expected since the muscles used are in pairs. Confirmation of this is found in pathological processes. If a cerebral abscess occurs in the region of a speech centre, speech will be completely lost when the presumed dominant centre has been destroyed. But in early childhood speech will be gradually regained as the opposite side takes over control. But after the age at which cerebral anatomy has reached full development, perfect speech will not return. An opposite train of events is seen if the non-dominant centre is destroyed by the abscess.

Since reversal symptoms occur between ear and hand when the dominant centres are on opposite sides of the brain, it may be reasonably presumed that reversal following the transference from ear to speech indicates that the speech centre is on the side of the brain opposite from the dominant auditory centre.

In Experiments 5 and 6 it will be seen that with the vertical presentation no reversals occur. So, when the child reads or writes along a line more vertical than horizontal the dominant left eye is afforded less opportunity to act irregularly.

By combining the two main stimuli of hearing and sight, as in Experiments 7 and 8, reversals are again avoided, even though each stimulus of itself might lead to the symptom. The sound checks the movement of the eye, and prevents inaccurate perception. Then, accurate perception having been obtained at the visual level, this corrects any tendency to reverse from ear to hand or speech. In Experiments 13 and 14, the vision, being accurate, corrects the tendency of reversal from ear to expression.

Experiments 9, 10, 11 and 12 were planned to show the value of two forms of expression. It was found that any error made at the first stage of expression was repeated at the second, but that errors did not arise *de novo* in the second stage. The initial stimuli were, of course, single. When a child is reading his perception of the sense of a passage may correct what he has seen, or when he hears that he has said something absurd, he will look again and correct himself. This, of course, cannot occur when pure stimuli of sound or sight are used, though it is not uncommon in ordinary life.

Reversal symptoms may be avoided if the initial stimuli are multiple. For example, ear to writing does not reverse if emphasis and rhythm are added to the sound. The louder the sound, the less likely that only the dominant ear will be used. Similarly, vision will be accurate if the figures or letters are very large. It is often seen that some children add kinaesthetic memory to vision so that they can reproduce a design correctly. Irregular eye movements are avoided when the left-eyed child is prevented from using the eye in a left-right horizontal direction.

Treatment of Crossed Laterality

Transference of dominance from its natural side to the cerebral centre on the opposite side can only occur if the first centre is completely destroyed while the child is still very young. Similarly, but with more hesitation, the same may occur if the organ concerned becomes functionless. After the child has reached the pre-puberty age of 6 to 9 years full function is never regained. Such catastrophes cannot, of course, be reproduced as a form of therapy. Attempts to change the dominance by forcibly restricting the use of the dominant functioning organ—this is usually the hand—meet with varying degrees of apparent success. Forcible restriction of the use of the dominant hand does not stop the cerebral function, though the nervous impulses cannot find expression. As a result the function is initiated, first from one centre and subsequently from the other. This state of cerebral turmoil or indecision is shown in clumsy hand movements. The turmoil spreads and other centres are involved. For example, speech ceases to be the expression of one centre. The resultant stammer is comparable to putting two men on the driving seat of a coach and pair.

The degree of success depends upon the fixity of the original cerebral pattern and upon the intelligence of the child. If the intelligence is high, it may appear that there has been complete success, but these children always show some irregular dominance. Treatment must be aimed at overcoming the symptoms which handicap the child. A clue to this has been given by observing the compensations developed by intelligent children. The methods used have been amplified from experimental findings, and have proved successful in dealing with these handicapped children.

To prevent incorrect expression of what is heard it is necessary to avoid the single use of the dominant ear. In place of a soft monotone (as of a tired teacher) a full sound, with rhythm and emphasis must be made. This is easy with reading or the lecture type of lesson, but there are sometimes difficulties when figures are read either by the child or the teacher. This difficulty has been satisfactorily met by adding a musical memory. Each figure has its own musical pitch thus:

The number 9461 would then be read as:

This does not involve any musical ability, and can be used by a child even when reading silently. Reversal is absolutely avoided.

The problem of accurate expression of what is seen is approached differently. Where hand and eye have opposite dominance, writing can be made easier and more regularly formed if the child is taught to turn the book and write obliquely. The child with /LR/ should write away from himself, and with /RL/ towards himself. Reading for these children can also be made easier if the book is held obliquely. Reading for content must not be hurried until the child has overcome the handicap entirely. These children should not be expected to read alone problems written on a blackboard, especially if numbers are involved. While the child looks at the board, the teacher should read the problem using correct emphasis, and the musical notation for numbers. After a period, the length of which will vary with the type of cerebral irregularity and the child's intelligence, it will be reasonable for the child to work alone.

When incorrect perceptions have already become common the child will have difficulty in spelling, a difficulty which increases rather than being overcome. The essential need is to obtain a correct appreciation of the form of the word. This may be done by considering the word as a design which is to be reproduced and adding kinaesthetic to visual memory. The word should be written by the teacher on a strip of paper in large (1 to 2 inches) copperplate letters. The child then traces over these letters, using the whole arm, and keeping the finger tip on the writing he is following, while the word is pronounced in letters or syllables. This is done several times until the child is sure of the word. There is nothing to be gained by hurrying, and making a mistake is a backward step. Unless the child is certain he should return again to the copy. This usually results in a noteworthy improvement quite quickly, but it must be remembered that there is probably a debit balance of bad spelling to be erased from the memory. New words will be learned more quickly than old words which have been fumbled or always spelt with one persistent error. This method of learning new words must be used almost indefinitely. If it is neglected the child drops back into all the old troubles in the course of a few months. The advice that children should write the

word in the air or on the desk before they do so on paper does not meet this difficulty. When the child does this he is expressing what he has perceived, not correcting his perception by the addition of kinaesthetic sense.

When it can be shown that the child has ability to use both hands he should be trained to use first of all the hand that brings dominance completely to one or other side. Thus, L L rl L should be taught to be L L L L and R R rl R should become R R R R. Having set the child to develop in this way, the ability of the other hand should not be suppressed, but encouraged to become a useful ancillary hand. Sometimes a child shows some degree of ambidexterity, but is so crossed that he cannot be trained into either complete left or complete right dominance. He should then be so taught that the hand of which is required the highest skill fits best into the pattern of cerebral dominance and produces minimal symptoms. For example, L L rl R will probably turn out best if he be trained to become L L R R. Then expression and reception are balanced. But if the position of the dominant speech centre is determined one can train the child into a more secure position; thus L L (L) rl R will do better as L L (L) L R while L L (R) rl R should be taught to become L L (R) R R. A watch should be kept lest the child shows any symptoms of distress and adjustment made accordingly.

Emotional disturbances will have occurred if symptoms have persisted for any length of time. This will respond to general treatment if the underlying cause is corrected. When the condition is found in the early stages of schooling (this is the time when diagnosis should be made) the child must be taught the way to compensate for the handicap, but at the same time the child, his teacher and his parents should understand that he is not abnormal in a pathological sense, but rather different from many, and with special abilities. When intelligent, older children are discovered who are failing at school or who have become lazy, a big advance will be made by explaining to them their handicap, and why they have failed. Demonstration to such a child of his real ability to reach the right answer, even where he has failed (as, for example, in spelling), when he uses the methods suggested is usually followed by a fresh, enthusiastic attack on his work, and he begins to take his proper place among other children.

Summary

Crossed laterality was found among children in a boarding school. Its prevalence and aetiology are examined.

The natural history and symptomatology are related to observed educational problems.

Experiments are described whose aim has been to discover the mechanism whereby the symptoms arise.

Effective treatment, which has been suggested by observation of the natural history of the condition and of experimental findings, is recorded.

I would acknowledge the kindness of the Lord God in giving this unique opportunity of studying His workmanship, and His guidance and help as problems have been spread before Him in prayer.

Thanks are due to the staff (teachers and others) of the Kuling School of the China Inland Mission for their willing cooperation in reporting difficulties and evaluating the treatment suggested; the late Mr. F. Mitchell, English Home Director of the China Inland Mission, gave permission for the presentation of this report.

ACCIDENTAL POISONING IN CHILDHOOD

BY

J. O. CRAIG and M. S. FRASER

From the Royal Hospital for Sick Children, Edinburgh, and the Department of Child Health, University of Aberdeen

(RECEIVED FOR PUBLICATION MARCH 25, 1953)

A recent increase in the number of children brought to hospital with accidental poisoning has been noticed in Edinburgh and Aberdeen. In a study of this trend, which has also been recorded in Manchester (Holzel and James, 1951), we have tried to determine whether it reflects a true increase of poisoning in the child population. We have then compared the incidence of the individual toxic agents and the mortality from each in order to show which poisons are most in need of control.

Material

Five hundred and two case-records have been examined of children under the age of 12 years who were accidentally poisoned in the years 1931 to 1951 inclusive. Two hundred and sixty-five were seen at the Royal Hospital for Sick Children, Edinburgh, and 237 at the Royal Aberdeen Hospital for Sick Children. The cases from these two hospitals were found to be so similar, both in frequency and in the types of poison swallowed, that it has been possible to combine them as a single source of material. In addition, the Registrars-General have provided us with the certified causes of death of 454 fatally poisoned children.

Poisoning by gas or smoke and bacterial food poisoning have been excluded, and also poisoning which occurred while a known therapeutic risk was being taken. We have discarded as harmless such incidents as the swallowing of insulin or soap, but have included all those in which poisonous substances were reputedly taken, whether symptoms occurred or not. In-patients and out-patients have been considered together, as a distinction between them depends partly on circumstances, such as the time of day at which a child reported. One hundred and thirty-one of the Edinburgh children were admitted and 110 in Aberdeen.

On all but one occasion (an accidental overdosage by injection), the poisons were ingested. Most of the cases were mild, and only two children died, one of morphine and one of methyl salicylate poisoning. When a child returned after taking poison on a second occasion, the incidents have been recorded as separate cases. This happened only twice; there were 502 poisonings which concerned 500 children.

The figures on which our diagrams are based are grouped in Appendix A, and the statistical analyses of the graphs will be found in Appendix B.

Incidence

In 1931 about five cases were brought to the hospitals each year; by 1951 the number had risen to more than 50 (Fig. 1). This tenfold increase is

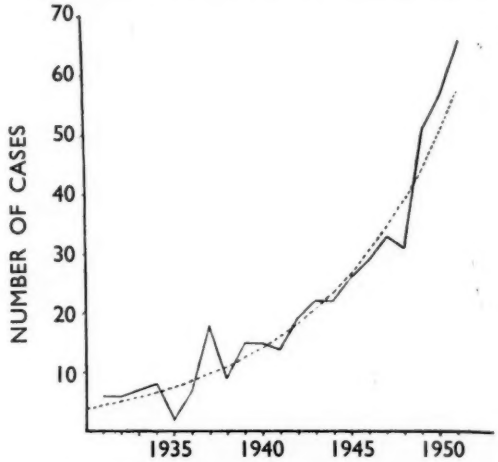


FIG. 1.—All poisoning cases, Edinburgh and Aberdeen. Average time-trend shown as dotted line.

striking, but does not in itself indicate that there has been a rise in poisoning in the child population. Social changes may have been largely responsible, causing parents to bring their children to hospital more readily. The effects of such changes can be assessed indirectly, in two ways: (1) By taking into account the general increase in the work of the hospitals; (2) by comparing the incidence of poisoning with that of a similar domestic accident, burns and scalds.

Further evidence on the reality of the increase can be obtained: (1) By studying the national mortality

from poisoning; (2) by classifying the hospital cases according to the source of the poison.

Hospital Turnover. Is the increase in the number of poisoned children attending hospital simply a reflection of a general increase in the use of hospital facilities? Fig. 2 shows that, even in relation to the hospital turnover, there has been a fivefold rise in poisoning. By its magnitude this rise suggests a true increase of poisoning in the population. If there were a growing tendency to bring trivial cases to hospital, those seen in recent years would be expected to be less severe than the earlier ones. Classification according to the severity of poisoning proved to be impracticable, but a bald comparison of those who developed symptoms and those who did not, produced no evidence that the poisonings now seen are less severe than they used to be.

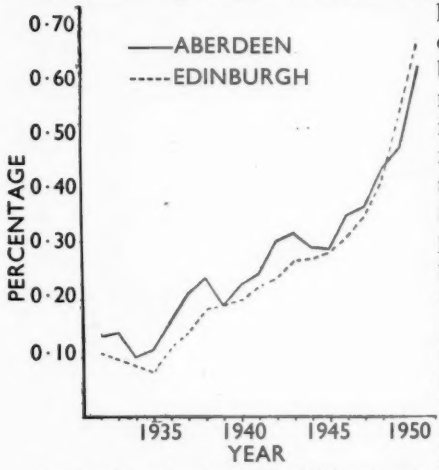


FIG. 2.—All poisoning cases, Edinburgh and Aberdeen, shown as percentage of turnover of appropriate departments.

Burns and Scalds. Burns and scalds resemble poisoning in that they are domestic accidents, are often very mild, and affect a similar age group. Only the Aberdeen hospital figures have been used, as there has been a campaign in Edinburgh against burning accidents. In Fig. 3 it will be seen that burns and scalds have increased by 150% (from 100 to 265 cases per annum) during the 21-year period. The relative rise in poisoning has been far greater, but the difference in the numerical strength of the two groups is so obvious that comparison on a percentage basis is scarcely justified. Of undoubted importance, however, is the fact that these household accidents have not increased in the same manner; the rise of burns and scalds has been linear, but that of poisoning curvilinear.

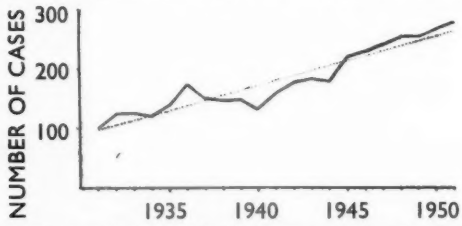


FIG. 3.—Burns and scalds, Aberdeen. Average time-trend shown as dotted line.

Mortality. Any true increase of poisoning should be reflected in the numbers of deaths from this cause. Close correspondence cannot be looked for, since the death rate can readily be affected by such factors as improved treatment and changes in the common types of poison. Swinscow (1953) has suggested that alteration in methods of certification may have been important after 1940, but the influence of this appears doubtful.

The annual numbers of deaths in Scotland are too small for reliable analysis, but the outlines of the British and Scottish mortality figures (Fig. 4) are so similar in their general characteristics that it seems justifiable to compare our morbidity figures with the British mortality. Swinscow, taking account of population changes, found no firm evidence of a continuing rise in poisoning deaths after 1940. When a longer period is considered, however, the impression of an increase dating from 1935 becomes clear, and this is strengthened by the previous long period of decline (Fig. 5). There is no evidence that toxic agents of recent introduction have caused the higher mortality, and the figures since 1935 are thus

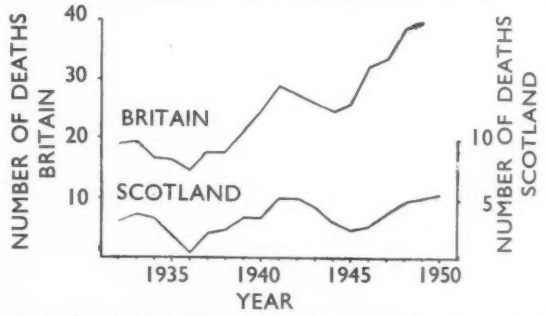


FIG. 4.—Deaths from poisoning in childhood, Britain and Scotland, shown as three-year moving averages.

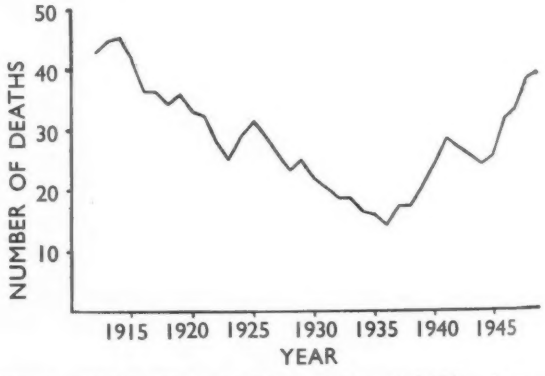


FIG. 5.—Deaths from poisoning, Britain, 1912-1949, shown as three-year moving averages.

compatible with an increase of poisoning among British children.

Sources of Poison. The 502 cases have been classified as follows:

GROUP 1.	Household substances, e.g., disinfectants, fuels, cleaning agents, insecticides	(203)
GROUP 2.	Medicines.	
	2A. Those intended for internal use	(185)
	2B. Those intended for external application, e.g., liniments, nose and eye drops	(75)
GROUP 3.	Vegetable matter, e.g., berries, seeds ..	(35)
GROUP 4.	Source unidentified	(4)

Cases due to a single toxic agent may contribute to more than one group, e.g., those due to atropine are divided between Groups 2A, 2B and 3.

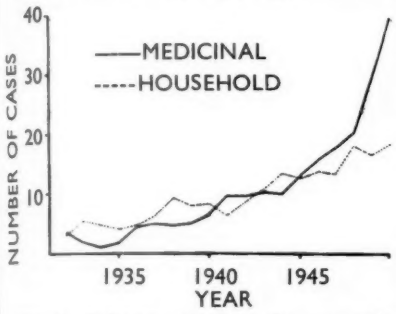


FIG. 6.—Poisoning cases in the two main groups, Edinburgh and Aberdeen, shown as three-year moving averages.

When the general trends of the two large groups are examined it appears that medicinal poisoning has recently increased much more rapidly than the household group (Fig. 6). This is of such importance that the two groups will be considered separately. The increase in poisoning due to household substances (Fig. 7) has been steady and linear, like that

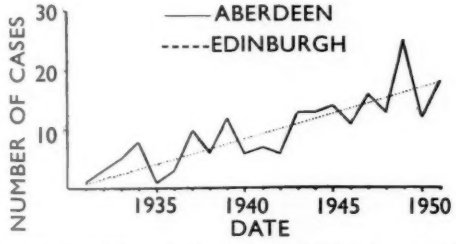


FIG. 7.—'Household' poisoning cases, Edinburgh and Aberdeen. Average time-trend shown as dotted line.

of burns and scalds; it seems that it is to this group of poisons that burns and scalds are most comparable. Yet the percentage increase in the household group has been about four times as great as that of burns and scalds, for what this type of comparison is worth.

In contrast to the household poisons, the medicinal group altered sharply in incidence about the year 1948 (Fig. 8). It is true that changes in population or social custom might have increased the hospital incidence of poisoning, for example, by diverting patients from the family doctor to the casualty department, but such a rise would not have affected the medicinal group alone. Some new influence is indicated.

From these lines of enquiry, it appears certain that a sharp rise in accidental poisoning has occurred since 1948 in the child population. A lesser increase in the period 1935-1948 is suggested, but the evidence for this is not conclusive.

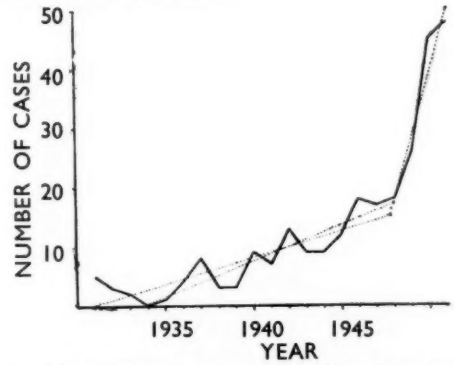


FIG. 8.—'Medicinal' poisoning cases, Edinburgh and Aberdeen Average time-trends shown as dotted lines.

Age and Sex. The age incidence of the whole series is shown in Table 1. The mean age for both Edinburgh and Aberdeen cases lay between 32 and 33 months.

TABLE 1
AGE INCIDENCE

Age in Years	Number of Cases	Age in Years	Number of Cases
Under 1 ..	25	6–7	13
1–2 ..	184	7–8	7
2–3 ..	147	8–9	9
3–4 ..	55	9–10	5
4–5 ..	30	10–11	3
5–6 ..	15	11–12	1

Age was not quoted in 8 cases. Total, 502.

In Fig. 9 (Edinburgh cases only) attention is directed to the early years of life. Although there is

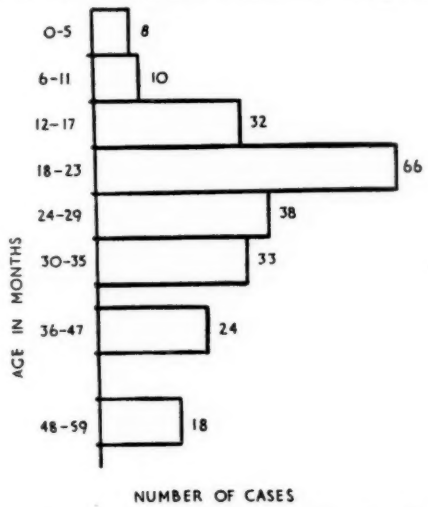


FIG. 9.—Age-incidence of poisoning in the early years, Edinburgh.

TABLE 2

ANALYSIS BY HOUSEHOLD POISONS

Number of Cases in Edinburgh and Aberdeen		Number of Deaths in Britain	
Disinfectants	39	Disinfectants	28
Kerosene	31	Caustic alkali	23
Turpentine	25	Phosphorus	17
Bleach	22	Ammonia	11
Ammonia	16	Kerosene	8
Dyes and inks	16	Acetic acid	6
Rat poison (phosphorus 4)	5	Arsenic, non-medicinal	5
Carbon tetrachloride	5	Nicotine	4
Potassium permanganate	5	Petrol	4
Caustic soda and potash ('Lye')	4	Cyanides	4
Petrol	3	Potassium bichromate	3
'Insecticide'	3	Soldering fluid (zinc and HCl)	3
Acetic acid	3	Hydrochloric acid	3
'Acid'		Metaldehyde	3
Shoe polish, paint, D.D.T., 'oil', of each	2	Potassium permanganate	3
		Turpentine, 'corrosive', sodium nitrate, carbon tetrachloride, copper sulphate, 'insecticide', sulphuric acid, of each	2
Varnish, corrosive sublimate, red squill, oxalic acid, lead, potassium bromate, soldering fluid, furniture polish, 'garden fluid', naphthalene, formalin, 'brasso', of each	1	Blue vitriol, 'cleaning fluid', oxalic acid, lead, sodium arsenate, potassium sulphide, zinc, zinc phosphide, benzine, 'paint solvent', window polish, antimony, methyl alcohol, 'paint-brush wash', mercuric nitrate, potassium chromate, of each	1

TABLE 3

MEDICINES INTENDED FOR ORAL USE EXCLUDING ATROPINE

Number of Cases in Edinburgh and Aberdeen		Number of Deaths in Britain	
Barbiturates	36	Strychnine	41
Iron (ferrous sulphate 21)	24	Iron	31
Salicylates	20	Quinine	20
Purgatives	15	Opium series	19
Opium series	10	Salicylates	19
Antihistamines	10	Barbiturates	10
Ephedrine	4	Digitalis	9
Thyroid	4	Antihistamines	6
Stilboestrol	4	Purgatives	6
Sulphonamides	3	Amidone, chloral, of each	2
Amidone ('physeptone')	3		
Amphetamine, ergot, isoprenaline, quinine, strychnine (in purgative tablets), of each	2		
Digitalis, mist. arsenic and ipecac., bromide, mandelate tabs., Lugol's iodine, nitroglycerine, chloral, pethidine, of each	1	Ipecacuanha, sulphone, 'irritant pills', 'kerol', of each	1

TABLE 4

MEDICINES INTENDED FOR EXTERNAL USE EXCLUDING ATROPINE

Number of Cases in Edinburgh and Aberdeen		Number of Deaths in Britain	
Camphor	29	Methyl salicylate (oil of wintergreen)	36
Iodine	11	Camphor	12
'Liniment'	6	Lethane	5
Sassafras	5	'Liniment'	2
Eucalyptus	4		
Methyl salicylate (oil of wintergreen)	3		
'Three oils', surgical spirit, of each	2		
Gentian violet, boric acid, 'eardrops', benzyl benzoate, calamine lotion, 'contraceptives', of each	1	Ol. citronella, iodine, eucalyptus, 'tar preparation' of each	1

TABLE 5

VEGETABLE MATTER EXCLUDING ATROPINE

Number of Cases in Edinburgh and Aberdeen		Number of Deaths in Britain	
Laburnum	15	Fungi	5
'Berries'	10	Water dropwort	4
Green elderberries	2	'Berries'	2
		Hemlock	2
Daphne berries, mistletoe, whinseeds, fungus, sycamore seeds, poppy heads, of each	1	Privet	1

TABLE 6
ATROPINE GROUP

Number of Cases in Edinburgh and Aberdeen		Number of Deaths in Britain	
Atropine eyedrops	5	'Belladonna'	8
Belladonna mixtures	2	Deadly nightshade	7
Deadly nightshade (clinical)	1	'Nightshade'	2
		'Atropine'	3
Hyoscine (medicinal)	6	Belladonna tablets	1
		'Hyoscyamus'	3
		Henbane (*Hyoscyamus niger*)	1
Woody nightshade (bittersweet)	1	Woody nightshade	3

a peak in the second year, poisoning is frequent throughout the pre-school years. There was no significant change in age incidence after 1948. The vegetable group of poisons affects older children; of 15 who had eaten laburnum seeds, for instance, the mean age was 5 years 9 months.

About three boys were poisoned for every two girls. This in itself is not significant, but it agrees with the figures of Ryan (1951) for sex incidence in Queensland and Swinscow's figures for mortality.

Frequency of Individual Poisons

In order to discover which poisons are most common in childhood and which are most lethal, Tables 2-6 have been drawn up to compare incidence and mortality. The incidence is derived from our 502 cases. The mortality is based on the deaths from accidental poisoning (excluding gas and food poisoning) of 454 British children under 10 years of age. Five hundred and one deaths occurred in the 21-year period (Fig. 4), but the certified causes are obtainable only for 401 in England and Wales in the years 1931-49 and for 53 deaths in Scotland in 1939-51. A few cases had to be excluded from the tables because the poisons were not named with sufficient accuracy.

These tables must be studied with an important reservation, that the comparison is between incidence in Scotland and mortality derived largely from England. Reasons have already been given for the quantitative use of the British mortality figures. That a qualitative use is also justified will appear in Table 7. This table shows the pattern of fatal poisoning in Scotland, and also shows that the Scottish and English patterns are remarkably similar. Crude as it is, this method of comparison provides useful information.

Table 2 shows that the most important household poisons are disinfectants, kerosene, caustic alkalies, and phosphorus (rat poison). The group of acids, excluding carbolic, accounted for 16 deaths. Turpentine and bleach are common poisons but are very seldom fatal; no death has been attributed to bleach in the last 20 years. Non-medicinal arsenic, potassium permanganate and carbon tetrachloride are uncommon poisons but carry a fair mortality.

Poisoning is not always recognized, and figures for the occurrence of lead, nicotine (usually insecticide), and cyanides, for instance, must be accepted with reserve.

Table 3 brings out clearly the importance of ferrous sulphate. The barbiturates and aspirin are prominent, and the toxicity of strychnine is particularly striking in view of its apparently low incidence. Digitalis and quinine are also rare but dangerous. A few deaths are attributed to purgatives, but some of these may have been due to other ingredients of compound tablets, such as atropine or even strychnine.

Camphor liniments are prominent in Table 4. Methyl salicylate (oil of wintergreen) resembles strychnine in that it is a rare poison with a very high mortality. Iodine is very seldom fatal, but lethane is dangerous.

In Tables 5 and 6 a direct comparison between incidence and mortality is not justified, owing to differences in flora between Scotland and England. Deadly nightshade is the most dangerous of the vegetable poisons, although uncommon in Scotland. Laburnum poisoning is common; death from this cause has been recorded, but is very rare.

The chief results of the preceding tables are summarized in Table 7, in which the virulence of a

TABLE 7
THE MAIN POISONS ASSESSED AS REGARDS POTENTIAL DANGER

Agent	Frequency (Edinburgh and Aberdeen)	Mortality (Britain)	Number of Deaths (Scotland)
Disinfectants	++++*	+++	8
Barbiturates	++++	++	0
Kerosene	++++	+	0
Camphor	+++	++	0
Turpentine	+++	+	0
Iron	+++	++++	7
Bleach	+++	—	0
Salicylates	+++	++	4
Ammonia	++	++	2
Atropine series	++	+++	0
Antihistamines	++	+	1
Opium series	++	++	2
Phosphorus	+	++	0
Strychnine	+	++++	8
Methyl salicylate	+	++++	6
Quinine	+	+++	3
Caustics ('lye')	+	+++	0

* An incidence or mortality of 1-9 cases has been scored as +, 10-19 = ++, 20-29 = +++, and over 30 = ++++.

particular poison can be roughly measured by the relation between the frequency of its occurrence and the frequency of death.

The Changing Incidence of Certain Poisons. In Table 8 the numbers of cases attending hospital due to the commoner poisons are shown in three-year groups. The household poisons (Nos. 1-5) have risen slightly, as have the medicinal applications (Nos. 6-7). In the group of internal medicines (Nos. 8-11), only the purgatives follow the trend of the household group; the others show a much steeper recent increase. The sharp rise in ferrous sulphate poisoning is not surprising, but it should be realized that the barbiturates and aspirin are increasing in a manner only slightly less striking. The figures for the vegetable group have risen unexpectedly in the post-war years. If there should prove to be a true increase in vegetable poisoning, this will remain to be explained. We can offer no convincing reason for it.

TABLE 8
THE INCIDENCE OF CERTAIN POISONS OVER A 21-YEAR PERIOD

Agent	1931–33	1934–36	1937–39	1940–42	1943–45	1946–48	1949–51
Disinfectants	4	4	5	6	8	2	10
Kerosene	0	1	4	3	11	2	10
Turpentine	2	1	6	0	4	6	6
Ammonia	0	1	2	1	3	5	3
Bleach	0	0	0	4	2	7	10
Camphor	3	0	3	8	6	3	6
Other applications	3	2	5	8	5	13	10
Purgatives	0	0	4	1	2	4	4
Aspirin	1	1	1	0	2	3	11
Barbiturates	0	0	0	4	3	9	20
Ferrous sulphate	0	0	0	0	1	4	16
Vegetable group	3	1	1	2	4	8	16

In looking for any trend in mortality, we have had to use the figures for England and Wales only in six-year groups (Table 9). The danger of attaching too much importance to these small figures is illustrated by the entry for methyl salicylate; a progressive increase in wintergreen poisoning is not probable, since 14 of these deaths occurred in 1944-45. There was a similar transient rise due to quinine, with eight deaths in 1940-41. On the other hand, the deaths from ferrous sulphate show a steady increase. It had been responsible for a considerable number of deaths before the danger of iron poisoning was generally recognized. The deaths of 17 British children were certified as due to ferrous sulphate poisoning in the 10 years before Forbes (1947) described it, and one child had died of ferric carbonate poisoning.

TABLE 9
NUMBERS OF DEATHS FROM CERTAIN POISONS, ENGLAND AND WALES

Agent	1932–37	1938–43	1944–49
Aspirin	2	5	9
Atropine (all sources)	8	4	6
Barbiturates	1	2	7
Disinfectants	5	9	4
Iron	1	6	18
Methyl salicylate	4	8	18
Morphine	4	6	7
Quinine	3	11	3
Strychnine	9	12	10
Vegetable poisons, including those containing atropine	6	4	15

The Principal Childhood Poisons. The only poison which is both common and very dangerous in Britain at present is ferrous sulphate. Indeed, had the mortality details been available for England and Wales in 1950-51, the figure for ferrous sulphate might well have been higher. The same applies to amidone and the antihistamines, drugs of recent origin which are dangerous to children.*

Two rare poisons, strychnine and methyl salicylate, are so virulent that they have caused the greatest numbers of deaths during the 21-year period and have taken a steady toll throughout. Strychnine is taken most often in the form of tonic or laxative tablets. Other poisons which are rare but dangerous are quinine, digitalis, morphine and phosphorus (rat poison).

The barbiturates are very common but carry only a moderate risk to life. It is probable that the toxicity of phenobarbitone in childhood has been exaggerated, since its danger in the individual case appears to be less than that of aspirin, household ammonia, or camphorated oil (Table 7). Kerosene is also common, but seems to cause few deaths. However, some deaths due to kerosene may have been registered under the lung complications.

Disinfectants are still commonly swallowed, but deaths due to this group have diminished with the substitution of less toxic substances for phenol and cresol. Caustic alkalies (lye), although apparently rare in Scotland, are common and dangerous elsewhere.

It is true that local custom and conditions modify the pattern of accidental poisoning. In California, for instance, the commonest toxic agent in childhood is an arsenical ant poison (King, 1950). Lye is the commonest in North Carolina (Arena, 1948) and Hungary (Csöke, 1948). Poisonings due to kerosene outnumber all others in Manila (Tupas and Dauis-Lawas, 1950) and Queensland (Ryan, 1951). Of 1,086 cases in Queensland, there was only one instance of ferrous sulphate poisoning, but this was the commonest poison recorded in Manchester by Holzel and James. It accounted for six of their 34 cases, most of which were due to medicinal sub-

* Since this paper was accepted we have received the following figures of deaths in England and Wales, under 10 years of age, in 1950-51: iron tablets 15, antihistamines 14, strychnine 10, aspirin 6, methyl salicylate 5, amidone 2.

stances. Bearing in mind such regional variations, we believe that our figures are broadly applicable to Great Britain.

Discussion

The Rising Trend. Evidence has been presented to show that accidental poisoning has been increasing in the child population, certainly since 1948 and probably since 1935. Some additional lines of investigation which did not invalidate this conclusion can now be briefly mentioned.

Variations in the toddler population of Edinburgh and Aberdeen in recent years were found to have been negligible by comparison with the increase of poisoning.

There has not been any considerable shift of cases from neighbouring hospitals; the records we have consulted show that the other hospitals have had a similar increase.

We have found no evidence that improvement in diagnosis has played a significant part in raising the hospital incidence, although some cases of iron poisoning may have been overlooked in earlier years.

It is obvious that the abrupt rise in medicinal poisoning occurred at about the same time as the introduction of the National Health Service, but it cannot be assumed that this was entirely a matter of cause and effect. For example, Ryan (1951) showed that poisoning increased sharply in Brisbane Children's Hospital from 1946 to 1949, although it is not clear how far this was due to medicines. Again, while prescribing has increased by 50% in Scotland since 1948, medicinal poisoning has been trebled. This difference is so great that a possible cause for it has been sought. If it were due to growing parental carelessness or a greater readiness to bring children for treatment, a comparable rise would be expected in poisoning due to household substances but the increase in household poisoning remains linear. It may be that many of the 'new' prescriptions have gone to homes where overcrowding and lack of experience in dealing with medicines might cause them to be poorly guarded. There has been a growing tendency to prescribe tablets rather than liquids. In Aberdeen in 1931 liquid medicines were dispensed twice as commonly as tablets, but since 1946 the two forms of prescription have been roughly equal in frequency (Fraser, 1953). Even when liquids were more in favour, tablets were the more frequent cause of poisoning (Appendix A). A relative increase in the dispensing of tablets would therefore raise the poisoning rate, but since this factor seems to have been fully developed before 1948, it cannot have played any part in the later rise.

The personality of the child who takes poison by accident remains to be considered. If emotional disturbance in early childhood were increasing, this might influence the poisoning rate. A child who feels insecure may revert to infantile behaviour, with a renewed tendency to transfer objects to his mouth. This is a very theoretical consideration, but should perhaps not be dismissed completely.

The one clear fact that emerges is that the rise in medicinal poisoning has occurred during a period of increased prescribing. It may reasonably be expected that, if the amount of prescribing becomes stabilized, the rapid increase in poisoning will cease.

Prevention. Poisoning is one of the minor accidents of childhood. For every child who dies from this cause, 20 are killed on the roads. Poisoning is on the increase, however, at a time when we are accustomed to diminishing diseases, and most of that increase is due to medicinal poisons. The problem is thus one for the medical profession in particular.

For the purpose of prevention, more information is needed. For example, it may be found that the rise which we have described, and which has been noted in Manchester, is characteristic only of large towns; the increase recorded by Ryan in Brisbane did not occur in the rural areas of Queensland. It is also possible that figures taken from children's hospitals do not exactly reproduce the national poisoning pattern (see Appendix C).

Too little is known about the circumstances in which poisoning occurs. In any enquiry, the following details should be included in the case history: (1) In what receptacle was the poison kept? For example, was it in a box or a screw-cap bottle, or was it in a receptacle intended for something else, such as kerosene in a lemonade bottle? (2) Was it under lock and key? (3) By whom was the poison given if it was not self-administered? (4) What are the social conditions, e.g., the number of persons per room? (5) What is the temperament of the child, and does the parent-child relationship seem to be good?

Preventive efforts in the meantime should be chiefly devoted to the medicinal cases, and the family doctor has an important part to play. He should ensure that the dangers of medicines are explained to their recipients, that medicines are dispensed in a form in which the danger is minimized, and that particular care is given to what medicines are prescribed in homes where there are young children. Parents must be encouraged to keep *all* medicines out of the reach of small children; even aspirin and laxative tablets are potentially lethal. A specific warning should be given when prescribing ferrous sulphate, strychnine preparations, and oil of wintergreen.

Summary

Among children attending two Scottish hospitals, accidental poisoning has become much more frequent during the past 20 years. An attempt has been made to determine whether this represents a true increase of poisoning in the child population. For the years 1935-48 the evidence favours this but is not conclusive. There can be no doubt, however, of a sharp general increase in the years 1949-51; it is chiefly explained by a rise in the accidental ingestion of medicines.

The poisons most commonly swallowed by Scottish children are disinfectants (not lye), barbiturates, kerosene and camphor liniments. Those which are most often fatal to children in Great Britain are ferrous sulphate, strychnine, methyl salicylate and the disinfectants.

We are greatly indebted to Professor R. W. B. Ellis and Professor John Craig for their advice and encouragement; to the Medical Superintendent of the Edinburgh Northern Group of Hospitals and to Dr. J. O. Forfar for giving us access to the records of the Western General Hospital and Leith Hospital; to Dr. D. N. Nicholson for allowing us to include cases under his care; to the Registrars-General for Scotland and England and Wales for supplying us with information not included in their reports; to Miss C. Brydone for her help in the preparation of the figures; and especially to Dr. Lilli Stein for detailed statistical guidance.

References

Arena, J. M. (1948). *J. Pediat.*, **32**, 208.
Csöke, L. (1948). *Népegészégügy*, **29**, 609. Abstract (1951) in *Amer. J. Dis. Child.*, **82**, 211.
Forbes, G. (1947). *Brit. med. J.*, **1**, 367.
Fraser, M. S. (1953). *Pharm. J.*, in the press.
Holzel, A. and James, T. (1951). *Med. Offr.*, **86**, 169.
King, A. L. (1950). *Permanente Fdn med. Bull.*, **8**, 20.
Ryan, D. C. (1951). *Med. J. Aust.*, **2**, 702.
Swinscow, D. (1953). *Archives of Disease in Childhood*, **28**, 26.
Tupas, A. V. and Dauis-Lawas, D. (1950). *Acta med. philipp.*, 7, 61

APPENDIX A

	Edinburgh				Aberdeen				Mortality		Mort. EW.		E. and Ab.		Ab.
Year	H.	M.	A.	V.	H.	M.	A.	V.	EW.	S.	H.	M.	T.	L.	BS.
1931	1	1	1	2	–	1	2	–	17	2	9	4	–	2	100
1932	–	2	1	1	3	–	–	–	19	1	9	5	2	–	122
1933	3	–	–	–	2	–	2	–	12	6	5	1	–	–	125
1934	4	–	–	–	4	–	–	–	15	4	6	6	–	–	131
1935	1	1	–	1	–	–	–	–	12	–	5	7	–	–	139
1936	–	2	–	–	3	–	2	–	16	1	7	8	1	1	173
1937	5	3	2	–	5	2	1	–	15	–	8	4	4	–	151
1938	3	1	1	1	3	–	1	–	16	5	6	6	–	–	149
1939	4	1	2	–	8	–	–	–	15	2	6	6	1	–	150
1940	3	4	4	–	3	–	1	–	22	3	7	10	3	1	135
1941	4	–	4	–	3	1	2	1	27	5	7	12	–	1	160
1942	2	6	2	1	4	2	3	–	23	7	11	7	7	1	178
1943	9	2	2	1	4	4	1	1	18	3	7	6	5	–	185
1944	8	3	2	–	5	1	3	1	18	3	6	3	3	1	180
1945	9	4	2	1	5	5	1	–	30	2	6	8	7	2	220
1946	6	6	5	–	5	6	1	–	23	2	6	12	8	3	230
1947	5	5	5	3	11	5	2	1	36	4	13	17	7	2	245
1948	6	9	2	4	7	5	2	–	31	5	15	13	14	–	255
1949	15	7	1	2	10	14	4	2	35	5	10	18	19	2	255
1950	4	21	3	4	8	18	3	2	39	5	?	?	33	6	266
1951	10	20	2	3	8	23	3	3	?	6	?	?	36	6	278

EW. = England and Wales. S. = Scotland. E. = Edinburgh. Ab. = Aberdeen. H. = Household poisons. M. = oral medicines. A. = medical applications. V. = vegetable poisons. T. = tablets, etc. L = liquids. BS. = burns and scalds.
Four cases of unknown poisons are excluded. In six instances of 'medicinal' poisoning, it is either not clear whether the poison was taken in liquid or solid form, or else the child was known to have taken both.

APPENDIX B

STATISTICAL ANALYSIS

The purpose of the analyses is to describe the average time-trend over the 21-year period for each set of figures, to compare these trends and to seek any significantly different or similar rates of increase.

Method

In those groups (Figs. 4, 5 and 6), in which only a general description is indicated and no further analyses or comparisons are made, the average time-trend is shown by three-year moving averages of actual numbers of cases or deaths. These moving averages compensate to some extent for annual fluctuations.

In those groups in which comparisons of rates of increase are made, lines or curves have been fitted by the method of least squares, and these lines will be discussed in detail.

Results

Poisonings from All Causes, Edinburgh and Aberdeen, 1931-1951. From the original figures, the mean = 22·0 and the standard deviation of mean = 17·2.

The curve which has been fitted indicates the trend

much more closely than a straight line, and in spite of the divergencies from the curve the correlation coefficient is 0·912. The S.D. from the average time-trend is 4·1, much lower than the S.D. of 17·2 from the 21-year mean.

The equation of the curve estimating the 'expected' number of poisoning cases is $P_e = 3{\cdot}909 \times (1{\cdot}137)^Y$ where Y = the year-number after 1930. The increments throughout have been on the average 13·7% of the previous year's total, meaning that in the early years there was less than one additional case per annum, but in the more recent years the increments averaged six to eight additional cases per annum. It is clear from the diagram that in fact the rate of increase in the last three or four years has been even steeper than that given in our equation, and the divergencies between the 'expectations' and the actual observations are most consistent in the years 1949-1951.

Burns and Scalds, Aberdeen, 1931-1951. The mean = 181·8, the S.D. of the mean = 53·3.

The equation of the fitted trend, giving an estimate of the average number of burns in terms of the year of occurrence is $B_e = 89{\cdot}5 + 8{\cdot}4Y$. The increase in the number of cases has been steady. The average number of additional cases per annum throughout the two decades has been between eight and nine. The 'expected' numbers correspond particularly well with the actual numbers treated in recent years. The divergencies from the average time-trend, e.g. the low figures in the early war years, are not in fact of great importance, as is evident from the correlation coefficient of 0·953. The S.D. from the average time-trend (16·6) is small compared with the S.D. from the 21-year mean (53·3).

Household Poisonings. The mean = 9·7, the S.D. of the mean = 5·9.

The equation of the line is $H_e = 0{\cdot}880 + 0{\cdot}799Y$. The numbers fall into a fairly regular pattern, and the time-trend is one of steady increase between 1931 and 1951. The 'expected' numbers often differ from the actual numbers, but they agree extremely closely with the 3-year moving averages. The increase in household poisonings averaged 0·8 added poisoning cases each year. The divergencies of the 'expected' numbers are relatively unimportant, as can be seen from the correlation coefficient of 0·826. The S.D. from the average trend is 3·4, as compared with the S.D. of 5·9 from the 21-year mean.

Medicinal Poisonings. The mean = 12·4, the S.D. of the mean = 12·8.

No curve was found to describe the fitted trend as well as the pair of straight lines, which have a correlation coefficient of 0·847. The medicinal poisonings followed a steady upward trend during the period 1931-47 ($M_e = 0{\cdot}9044Y - 0{\cdot}9044$), similar to the household poisons. The two coefficients of Y are very similar. The trend of medicinal poisonings then changed abruptly, and between 1948 and 1951 is represented by the equation $M_e = 10{\cdot}9Y - 178{\cdot}3$. The S.D. from the average time-trend is 2·9, a remarkably low figure compared with the S.D. of 12·8 from the 21-year mean.

In Fig. 8 the average time-trend for the period 1935-47 is also shown. This line allows for the possibility that the period 1931-35 was a period of fall, but differs very little from the 1931-47 line.

Up to 1948, the average increment was nearly one additional case per annum, but since 1948 it has been nearly 11 added cases per annum. The difference between these two rates of increase is highly significant.

Conclusions

The similarity between the burns and the household poisonings lies in the fact that both have an average trend which is linear. On the other hand, there has been a distinct change in the trend of the medicinal poisoning cases. It is not suggested here that there is a causal connexion between that change in the trend and the period in which it seems to have occurred.

LILLI STEIN,

Department of Social Medicine, University of Edinburgh.

APPENDIX C

A NOTE ON LEITH HOSPITAL

Leith is the port of Edinburgh. The general hospital there draws its patients largely from crowded tenements, and differs in that respect from the children's hospitals of Edinburgh and Aberdeen where the patients represent almost all social grades. It has about 25 beds for children, and 73 cases of poisoning were admitted between 1931 and 1951. This small series has been tabulated in three-year groups:

Source of Poison	1931–33	1934–36	1937–39	1940–42	1943–45	1946–48	1949–51
Household ..	2	2	3	6	4	8	7
Medicinal ..	1	3	3	3	5	9	14
Vegetable ..	1	0	0	0	0	1	1
Total ..	4	5	6	9	9	18	22

The figures are small and take no account of out-patients, but they do show the general rising trend and the recent medicinal preponderance, although the latter was not clearly seen until 1950.

The common poisons at Leith were camphor (10 cases), ammonia (six), bleach (five), disinfectants (four) and petrol (four). The commonest medicinal poisons were aspirin, the opium group and digitalis (three cases of each). Strychnine poisoning occurred once and was due to Easton's tablets; it caused the only death among the 73 cases.

The pattern of individual poisons is rather different from that found in the two hospitals for children. It suggests that the social groups which a hospital serves may help to determine the variety of poisonings seen there. The difference is not gross, but it should receive attention in any future enquiry.

THE ESTIMATION OF BLOOD PRESSURE IN CHILDHOOD WITH SPECIAL REFERENCE TO THE CHOICE OF STANDARD CUFFS

BY

H. SAINSBURY

From the Herefordshire Child Health Centre, Hereford

(RECEIVED FOR PUBLICATION APRIL 7, 1953)

In adults the sphygmomanometer gives blood pressure readings similar to those obtained directly with a canula in the artery (Steele, 1942) provided that the inflatable cuff used is of suitable dimensions, i.e., 12 cm. broad (von Recklinghausen, 1901). Smaller cuffs yield high readings (Gumprecht, 1900; Janeway, 1909; Phipps, 1915; Day, 1939) especially in high tension pulses (Hutchison and Rainy, 1924) and broader cuffs may give low readings (Cook, 1903; Robinow, Hamilton, Woodbury and Vopitto, 1939). The length of the cuff in relation to the circumference of the arm is a matter on which opinions have differed and is probably of much less significance. In view of the wide variation in the size of children's arms difficulty has been experienced in obtaining agreement on the most suitable dimensions for standard children's cuffs. Nicholson (1915) recommended for children of 4 to 8 years a cuff 9 cm. broad and for children 8 to 15 years one 13 cm. Robinow *et al.* (1939) recommend a cuff 2·5 cm. broad for the newborn, 5 cm. for small children, and 9 cm. for older children. The American Heart Association (1951) recommends cuffs 8-9 cm. for older children under 9 years, 5-6 cm. for children under 4 years, and for infants under 1 year 2·5 cm. Taussig (1940) suggests that the breadth of the cuff should be two-thirds the length of the upper arm. This appears to be generally accepted by paediatricians in Britain.

Although certain writers (Day, 1939; Allen-Williams, 1945) have folded the rubber bag within the cuff in such a way as to adjust its breadth to the size of the arm, the method is not convenient in clinical practice where it is usual to employ cuffs of standard sizes. In this country there are available three standard sizes of cuff, namely 1 in. (2·5 cm.), 2 in. (5·0 cm.) and 4 in. (10 cm.) in breadth. The adult cuff measures 5 in. (12·5 cm.).* It is the purpose of this paper to ascertain how far these cuffs may be employed to obtain comparable blood pressure readings.

The dimensions of these cuffs were no doubt originally based on experiment, but appear now to be determined by demand, and no information could be obtained from the instrument makers concerning the ages for which they are intended.

It is more convenient to refer to the size of children in terms of age, and for this purpose mean values for the length of the upper arms of children at different ages were obtained and are presented in Table 1. The measurements were taken from the fold of the axilla to the centre of the antecubital space with the arm semiflexed and the forearm supinated.

In Fig. 1 the histogram represents the length of arm which should be enclosed by the cuff, i.e., two-thirds of the mean arm lengths in Table 1, to give blood pressures comparable at one age with another. The breadths of the 5 cm., 10 cm., and adult cuffs

TABLE 1

AVERAGE MEASUREMENTS OF UPPER ARM OF CHILDREN AGED 1-17 YEARS*

Age of Child	Mean Arm Length (cm.)	Range of Values (cm.)	Variability (S.D.)
6-12 months	6·5	7–5·5	0·8
2nd year	9·3	9–10	0·8
3rd ,,	10·5	9–13	0·8
4th ,,	11·4	9·5–13	0·7
5th ,,	12·5	10–15	1·0
6th ,,	13·0	11–16	1·25
7th ,,	14·0	12–16·5	1·2
8th ,,	14·0	12–15·5	1·0
9th ,,	14·5	12·5–17	1·3
10th ,,	14·8	13–17	1·4
11th ,,	15·0	14·5–19	1·25
12th ,,	16·0	14·5–18	1·06
13th ,,	17·0	14–19	1·3
14th ,,	17·5	15–20	1·3
15th ,,	18·5	16–24	1·37
16th ,,	19·0	15–22	1·5
17th ,,	19·1	16–24	1·7

* Derived from samples of 20 boys and 20 girls in each age group.

* Other cuffs, e.g., 7, 9·5 and 12 cm., are also available [ED.].

(shown as shaded areas) are superimposed to emphasize the differences between the required breadth and that of the standard cuff which most nearly approximates to it. Where alternative standard cuffs exist the larger has been shown. It will be seen that a material discrepancy occurs in the age intervals 2-6 years and 12-13 years.

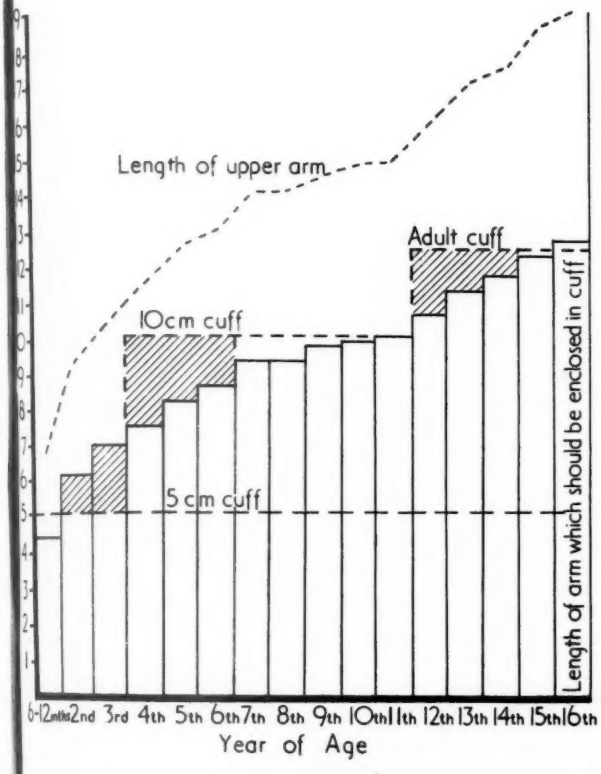

Length of upper arm
Adult cuff
10cm cuff
5 cm cuff
Length of arm which should be enclosed in cuff !
6-12mths 2nd 3rd 4th 5th 6th 7th 8th 9th 10th 11th 12th 13th 14th 15th 16th
Year of Age

FIG. 1.—Illustration of the extent to which standard cuffs are applicable to the arms of children aged 1-16 years.

The effect of these discrepancies on blood pressure readings was examined by subjecting samples of children to examination using both the standard cuff and one folded to enclose exactly two-thirds of the arm. Mean differences between the pairs of readings are shown in Table 2.

The children were examined in accordance with the recommendations of the Cardiac Society of Great Britain and the American Heart Association (1939). The instrument used was a standard type of mercurial manometer. The cuff was folded in the manner described by Day (1939). Each examination consisted of a series of readings taken alternatively with the standard and folded cuff until they became relatively constant.

The size of the samples was governed by the variability of the differences between the pairs of readings to yield a standard error of 1 or less.

TABLE 2

DISCREPANCIES BETWEEN PAIRS OF READINGS OBTAINED WITH A STANDARD CUFF AND ONE TWO-THIRDS THE LENGTH OF THE ARM AT CERTAIN AGE INTERVALS

Size of standard cuff (cm.)	5		10		12·5
Size of folded cuff (cm.)	7	7·5	8	8·5	11
Length of upper arm (cm.)	10	11	12	13	16–17·5
Age of children (yrs.)	2 and 3	4	5	6	12–14
No. of children examined	50	33	33	34	56
Systolic Readings					
Range of pressures (mm. Hg)	80–120	78–140	80–135	80–135	92–145
Mean difference between readings (mm. Hg)	8	7	5·4	4·7	3·3
Range of differences (mm. Hg)	0–16	1–12	0–15	0–20	0–15
Standard error (±)	0·5	0·5	0·6	0·4	0·3
Diastolic Readings					
Range of pressures (mm. Hg)	55–88	60–90	45–90	40–90	55–95
Mean differences between readings (mm. Hg)	6	7	4·8	4	5
Range of differences (mm. Hg)	0–20	0–20	0–15	0–20	0–10
Standard error (±)	0·42	0·57	1·0	0·6	0·6

Conclusions

It will be seen in Fig. 1 that the 10 cm. cuff can be applied to the arm of all children over the age of 3 years, but it particularly approximates to the required dimensions between the ages of 7 and 11 years. Between 4 and 6 years the cuff is somewhat large and gives readings on an average 4-7 mm. Hg (according to age) lower than those obtained with a cuff strictly proportional to the length of the arm. Similarly in the twelfth and thirteenth years the cuff is small and readings higher than they should be.

Although strictly speaking the adult cuff should be reserved for children of 15 years and over, it may with advantage be employed to obtain more stable results in the age periods of 12 years and over. In the twelfth and thirteenth years systolic readings obtained with this cuff are low by 3·3 mm. Hg.

Below the age of 4 years only the smallest cuff will fit the arm but at three years this cuff is somewhat small and readings are found to be 8 mm. Hg systolic and 6 mm. diastolic higher than those obtained with a cuff exactly two-thirds of the arm length.

Individual differences between pairs of readings

varied within 20 mm. Hg, and this should be viewed against the usual range of normality. Pairs of high readings showed no obvious tendency to greater discrepancy than did lower readings throughout the range of pressures observed.

Summary

An attempt has been made to ascertain to what extent the standard sizes of inflatable cuffs normally available are applicable to children of different ages, presuming that to obtain comparable readings they should enclose two-thirds of the upper arm of the children for whom they are intended.

Mean values for the size of children's arms at different ages are presented, and it was found that the 10 cm. cuff can be used for all children between 4 and 12 years. Below 4 years only the 5 cm. cuff will fit, but children over 12 years can take the adult cuff.

In those age ranges in which these cuffs departed materially from the requirement of enclosing two-thirds of the upper arm readings taken with the standard cuff and with a cuff folded to comply with this requirement were compared. The discrepancies, while they varied in individual cases from 0 to 20 mm. Hg, were generally small.

I wish to thank Dr. Cookson, County Medical Officer, and Dr. Hugh Fisher, Consultant Paediatrician to the Herefordshire Child Health Centre, for permission to publish this paper and for their helpful suggestions in its preparation; also Mr. Gordon Cossor, of A. C. Cossor Ltd. for information concerning the manufacture and supply of the cuffs.

References

Allen-Williams, G. M. (1945). *Archives of Disease in Childhood*, **20**, 125.

American Heart Association (1951). *Circulation, N.Y.*, **4**, 503.

Cardiac Society of Gt. Britain and American Heart Association (1939). Reported in *Brit. med. J.*, **2**, 184.

Cook, H. W. (1903) *Amer. J. med. Sci.*, **125**, 433.

Cossor, G. Personal communication.

Day, R. (1939). *J. Pediat.*, **14**, 382.

Hutchison, R. and Rainy, H. (1924). *Clinical Methods*, 8th ed., p. 192. London.

Taussig, H. B. (1940). In Holt's *Diseases of Infancy and Childhood*, 11th ed., p. 557. New York.

Janeway, T. C. (1909). *Arch. intern. Med.*, **3**, 474.

Nicholson, P. (1915). *Blood Pressure in General Practice*, 3rd ed., p. 134. London.

Phipps, C. (1915). *Boston med. surg. J.*, **173**, 476.

Recklinghausen, H. von (1901). *Arch. exp. Path. Pharmak.*, **46**, 78.

Robinow, M., Hamilton, W. F., Woodbury, R. A. and Vopitto, P. P. (1939). *Amer. J. Dis. Child.*, **58**, 102.

Steele, J. M. (1942). *J. Mt Sinai Hosp.*, **8**, 1042.

FOURTEEN CASES OF IDIOPATHIC MYOCARDITIS IN INFANTS AND CHILDREN

BY

HOWARD WILLIAMS, R. N. O'REILLY and ALAN WILLIAMS

From the Departments of Clinical Research and Pathology, The Children's Hospital, Melbourne

(RECEIVED FOR PUBLICATION MARCH 16, 1953)

The purpose of this paper is to present 14 case histories of infants and children with 'idiopathic' myocarditis in order to clarify the clinical and pathological features of the disease, to show how a diagnosis can be established, and to point out some common errors in diagnosis.

Idiopathic myocarditis was first described in 1899 by Fiedler in an adult patient, and during the next 30 years isolated reports of affected children and adults were recorded, mainly in the continental literature. Following a paper by Scott and Saphir in 1929 in which they reviewed the literature of 30 cases and reported two additional adult patients, a number of case reports in infants and children appeared in the American literature (Kenny and Sanes, 1933; Maslow and Lederer, 1933; Smith and Stephens, 1938; Greenebaum, Felson and Zeligs, 1941). In 1944, Saphir, Wile and Reingold reviewed all types of myocarditis in children and recorded the clinical and post-mortem data of 97 patients, three of whom had idiopathic myocarditis. The conclusions from this review were that there was little known clinically about idiopathic myocarditis which was usually unsuspected during life and not infrequently caused sudden death. The clinical findings, such as were available, suggested that the outstanding signs and symptoms were tachycardia out of all proportion to temperature, cyanosis and cardiac enlargement. The few patients who had electrocardiographic tracings showed flat, isoelectric or inverted T waves in the three standard leads. The morbid anatomical changes were an enlarged heart, often with hypertrophy, and an interstitial inflammatory reaction in the myocardium which frequently showed toxic and degenerative changes. There was rarely any evidence of pericarditis or endocarditis. Saphir *et al.* further stated that the aetiology was unknown, and clinically and pathologically the lesion was not associated with any known infection. Bacteriological examination of the heart and other tissues gave negative results, and pathological lesions were not detected in other organs. However, the pathological lesions in the myocardium were identical with those seen in some of the infectious diseases. An allergic basis and also an association with status thymicolymphaticus had been postulated by a few workers, but the evidence for this was inadequate. Clinically and pathologically the disease in no way resembled rheumatic infection.

Over the past eight years reports of a series of six cases by Keller in 1945, and of five cases by Lind and Hultquist in 1949 have helped to establish a better clinical picture of the disease. Keller described the features of rapid distressed breathing and cyanosis, tachycardia out of all proportion to the temperature, an enlarged liver, a grossly enlarged heart radiologically, and changes in the T waves in the electrocardiogram. Four of the five patients reported by Lind and Hultquist were under the age of 1 month and three of them had paroxysmal tachycardia.

Clinical and Pathological Material and Methods

Over the past three years, August, 1949, to December, 1952, 14 patients with idiopathic myocarditis have been studied, 12 of them at the Children's Hospital, Melbourne, and two in the Hamilton Base Hospital, Victoria. All patients were carefully observed clinically and electrocardiographic and radiological studies of the heart were made in most. In those patients who died routine macroscopic and microscopic examination was made of all organs, and histological study of the heart included sections from both ventricles, auricles, the interventricular septum and valves.

Classification

Classification serves as a basis for presentation of the patients rather than as a means of separating them into definite groups with distinctive clinical and

pathological phenomena. Clinically every variant was seen from severe acute cardiac failure, which was frequently rapidly fatal, to less severe, more insidious subacute failure.

The patients will be discussed in two groups. 1. The acute type was characterized clinically by the sudden onset of severe cardiac failure. The pathological changes in the seven patients who died consisted of widespread myocardial damage and interstitial cellular inflammation. The two surviving patients recovered completely. 2. The subacute and chronic type was characterized clinically by a rather longer history and more gradual development of cardiac failure. The pathological changes in the one patient who died were essentially the same as those in the acute group. The four surviving patients all had some permanent cardiac damage.

The Acute Type

There were nine patients in this group, the ages ranging from 12 days to 5 years. The initial manifestations of the malady were commonly mild, the mother attributing them to a minor ailment. Some had slight fever and were irritable and difficult to manage, others were vaguely not well, while some refused their food, vomited or had loose stools. One had a sore throat, another a 'cold'. None of the patients were in contact with infectious diseases and the parents and other members of the family were well at the time the child became ill. These symptoms were present for a few days or a week before the onset of cardiac failure, when the child rapidly became seriously ill. Circulatory and respiratory embarrassment were the outstanding clinical features. Pallor was a striking feature and varying degrees of cyanosis were noted in all patients. Some were restless and had a rather apprehensive look, while others were apathetic. The skin was cold, frequently mottled, often clammy and occasionally wet, and the temperature was either subnormal, normal or slightly elevated. The respirations were rapid, often as high as 90 to 100 per minute, usually deep with a short expiratory grunt or slight wheeze. The chest was frequently barrel shaped from pulmonary emphysema. The percussion note over the entire chest was hyper-resonant and at times the upper margin of liver dullness was displaced downwards owing to the low position of the diaphragm. The breath sounds were harsh and in some patients crepitations were heard at the lung bases. The pulse rate was rapid, usually between 150 and 170 per minute, weak and thready, and the blood pressure low. Cardiac enlargement was always present but often could not be detected clinically as the rapid respiratory rate and restlessness of the infant made palpation of the apex beat impossible, and the emphysematous chest rendered percussion of the heart unreliable. Sometimes cardiac enlargement was suggested by palpable pulsation immediately below the xiphisternum in the epigastrium. The heart sounds were usually of poor quality, the second sound at the apex often being louder than the first, and in some gallop rhythm further indicated cardiac embarrassment. Cervical venous engorgement could not be determined with any degree of certainty because of the short, stumpy neck and restlessness in most infants. The liver edge was invariably three or four fingerbreadths below the costal margin, but could be overlooked unless palpation was begun well down in the lower half of the abdomen below the liver edge. The spleen was palpable in a few patients. Subcutaneous oedema was present in only two patients and in three the urine contained a trace of albumin but no red blood cells or casts. The overall clinical picture was that of an anoxic infant with severe circulatory failure and considerable respiratory distress. The clinical features of gross liver enlargement and minimal pulmonary congestion suggest that the cardiac failure predominantly affected the right ventricle.

Radiological examination of the chest showed gross uniform cardiac enlargement. In contrast to the large heart the lung fields were usually not congested, but were often hazy; this appearance suggested some oedema. In several patients small bilateral pleural effusions were noted, and one patient had an area of radio-opacity at one lung base suggesting either collapse or consolidation. The electrocardiogram showed serious impairment of myocardial function, the significant abnormal features being low voltage QRS complexes, especially in lead I, and low, iso-electric or inverted T waves in all three standard leads.

Necropsy showed that all hearts were dilated and the walls were usually thicker than normal. The only other macroscopic abnormalities were flabbiness of the heart muscle and irregular reddish or pale streaking in the muscle wall. With one exception the pericardium, endocardium and valves were all normal. Histological examination revealed widespread but often patchy damage of the myocardium, and an associated inflammatory reaction with neutrophil and eosinophil polymorphonuclear leucocytes, lymphocytes and macrophages.

Case 1. J.O'B., a boy aged 10 months, was admitted to the Children's Hospital on October 28, 1949, with a history of normal progress until three days previously when he was noted to be pale and rather drowsy. The

next morning he vomited and periodically throughout the day cried out as if in pain. These symptoms persisted and on the third day his respirations became rapid and grunting. Both parents and a brother aged 2 years were well and there was no contact with any infectious disease. Examination showed a well developed, slightly cyanosed infant who looked very ill and exhausted. The temperature was 98·4° F., the pulse rate 150 per minute, weak and thready, the blood pressure 70/50 mm. Hg and the respirations 80 per minute and grunting. The extremities were cold and mottled with extremely sluggish capillary circulation. The apex beat could not be felt, the heart did not seem to be enlarged by percussion, the sounds were distant and no murmur was heard. The liver was enlarged three fingerbreadths below the costal margin and there was no subcutaneous oedema or venous engorgement in the neck. The lungs were clinically clear, the urine and blood examination normal. The baby died after 24 hours without a clinical diagnosis being established.

Necropsy showed a symmetrically enlarged heart, congested and oedematous lungs and some serous fluid in both pleural cavities. The liver was enlarged and pale. The myocardium was diffusely infiltrated with leucocytes, mainly lymphocytes and plasma cells. These cells were aggregated around foci of muscle fragmentation. The liver showed patchy centrilobular necrosis with engorgement of the capillaries.

Case 2. E.D., a girl aged 15 months (weight 18½ lb.), was admitted to the Children's Hospital on June 19, 1950. Two weeks previously she had been vaguely ill and then for one week she had a slight cough with rapid breathing. Her parents, brothers and sister were well and she had no contact with any infectious disease. The infant was pale, looked ill, and the lips and extremities were slightly cyanosed. The respiratory rate was 90-100 per minute, the temperature 99° F., the pulse weak and thready at 170 per minute. The apex beat was difficult to define but forcible cardiac pulsation was present under the xiphisternum. No murmur was heard but gallop rhythm was present at the apex. The liver edge was palpable three fingerbreadths below the right costal margin and the tip of the spleen was palpable. The chest was rather emphysematous and a few fine râles were heard at both lung bases. Slight oedema was present in both feet and sacrum. The heart was considerably enlarged radiologically and the lung fields were clear. The urine did not contain albumin. Digitalis folium, grains 4 by mouth over 24 hours, and then grains ½ daily, was given together with oxygen. Forty-eight hours later the infant was very much improved. The colour was good, the pulse rate slower at 120 per minute, and the respiratory rate 36 per minute. The oedema had cleared, and the liver edge was palpable one-and-a-half fingerbreadths below the costal margin. Radiological examination five days after the beginning of treatment showed a heart which was much smaller. Digitalis was discontinued after 17 days. During the next two years the child developed normally and in August, 1952, the heart was normal clinically, radiologically and electrocardiographically.

Case 3. B.S., a girl aged 5½ years, was admitted on July 17, 1951, to the Hamilton Base Hospital. She had been off colour for five days with a sore throat and anorexia, had vomited for two days and had several convulsions on the day before admission. Both parents, her sister aged 3 years and brother aged 2 months, were well. The child had faucial diphtheria when aged 2 years, with palatal palsy but no evidence of cardiac involvement; recovery was complete, and she had been well since. Examination showed a healthy, well developed child. The temperature was 99° F., the pulse regular with good volume at 80 per minute, and the respirations 24 per minute. Slight tonsillitis was present and a throat swab grew *Streptococcus viridans*. The heart was clinically normal in size, the sounds regular and clear, and no bruits were heard. The blood pressure was 90/50 mm. Hg. The lungs were clear and the liver was not enlarged. The urine had a specific gravity of 1020, contained a trace of albumin, but was microscopically normal. A diagnosis of upper respiratory tract infection with tonsillitis and albuminuria was made, and treatment with penicillin, 100,000 units six-hourly, was given. The child's condition remained unchanged for 36 hours when unexpectedly at night the ward sister heard her cry out and observed a spasm of the arms and arching of the back. This spasm lasted approximately a minute, after which the child was pale, collapsed and sweating. Examination showed a shocked child, whose pulse was impalpable and whose blood pressure could not be recorded. The heart was not enlarged clinically. The ventricular rate was slow and slightly irregular with a rate of 20 to 30 per minute and faint auricular sounds were heard at 130 per minute. No venous engorgement in the neck or subcutaneous oedema was noted. The liver edge was palpable three fingerbreadths below the costal margin. An electrocardiogram showed a complete heart block (Fig. 1A). Treatment with oxygen, ephedrine, and adrenalin was ineffective, and gradually the circulation became worse, cyanosis pronounced, and the child died eight hours later.

Necropsy showed a slightly dilated heart with a flabby myocardium. The lungs were engorged and the liver enlarged with a nutmeg appearance. Histologically the myocardium showed patchy fragmentation of the muscle fibres accompanied by a cellular reaction consisting of eosinophil and neutrophil polymorphonuclear leucocytes, macrophages and lymphocytes (Fig. 1B).

Case 4. S.H., a girl aged 14 months (weight 16½ lb.), was admitted to the Children's Hospital on August 20, 1951, with a 'cold', slight fever and nasal discharge for five days. For two days her breathing had been wheezy, grunting and rapid, and her colour cyanotic. There was no contact with any infectious disease. Her past history revealed that at the age of 6 weeks she developed a staphylococcal lung infection which persisted in a subacute form over six months despite adequate treatment with penicillin and later with aureomycin. During this time she failed to thrive, her stools became greasy and a clinical diagnosis of fibrocystic disease of the pancreas was made. Skiagrams of the heart and lungs from the age of 6 weeks to 10 months showed a heart of normal size and lung changes compatible with bronchitis and

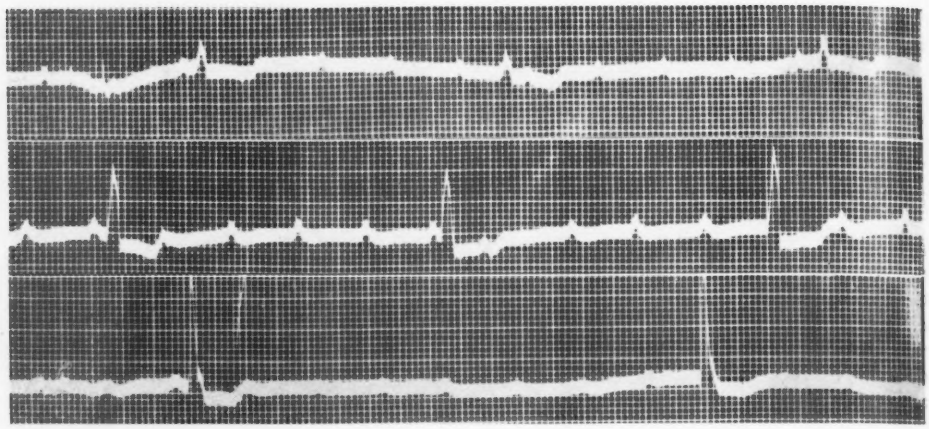


FIG. 1A.—Electrocardiogram showing complete heart block.

FIG. 1B.—Section from the interventricular septum showing diffuse muscle cell damage and cellular infiltration. ×110.

patchy pneumonitis. At 10 months of age she weighed only 13 lb. 10 oz., but over the next four months she improved steadily, took her feeds well, gained weight and her cough cleared. Examination on admission revealed a distressed, sick infant with rapid, wheezy respirations at 56 per minute, a temperature of 99° F., and pulse rate of 136 per minute. Clinically the heart was considered to be normal, but a skiagram of the chest showed gross symmetrical enlargement of the heart with slight pulmonary congestion. Scattered râles were heard at both lung bases with expiratory ronchi, and abdominal examination revealed no abnormality. A diagnosis of bronchopneumonia was made and treatment with penicillin and streptomycin given. The infant unexpectedly collapsed and died two days later.

Necropsy revealed a dilated heart with flabby myocardium. The lungs showed macroscopic and histological changes of bronchiolitis with pulmonary congestion at the bases. The pancreas was normal. Microscopically the heart muscle showed much fragmentation and diffuse mononuclear cell infiltration.

Case 5. J.L., a girl, aged 4½ years, was admitted to the Hamilton Base Hospital on September 10, 1951, with a provisional diagnosis of acute appendicitis. The child was well until the day of admission when she developed abdominal pain, lost her appetite and vomited. Examination disclosed a sick girl with a slightly enlarged heart, a soft, apical, systolic bruit and an enlarged, tender liver. The following day the liver was further enlarged to three fingerbreadths below the costal margin and the apex beat was in the fifth left intercostal space outside the nipple line. The temperature was 102° F., the pulse rate 140 per minute, the respirations rapid and grunting at 50 per minute, and the urine normal. Over the next three days the child's condition slowly deteriorated. The respirations were then rapid and grunting, the liver enlarged four fingerbreadths below the costal margin and crepitations appeared at the left lung base. Digoxin, 0·25 mg. statim and 0·125 mg. six-hourly, was begun, but death occurred 20 hours later.

Necropsy revealed a dilated heart (weight, 135 g.) with pale but firm muscle and a small serous exudate with fibrin clot in the pericardial sac. The lungs were congested and oedematous and the enlarged liver (weight, 765 g.) had a nutmeg appearance. Histologically widespread foci of myofibril damage with an accompanying cellular reaction of lymphocytes, macrophages and scattered polymorphonuclear leucocytes were found throughout the myocardium. In the region of the attachment of the mitral valve to the atrioventricular ring there was a relatively large area of infiltration with polymorphonuclear leucocytes and a small area of lymphocytic infiltration was present near the base of the valve.

Case 6. J.B., a boy aged 3 weeks (weight 6 lb.), was admitted to the Children's Hospital on February 9, 1952. He was a normal full term baby, the first child of healthy parents, and the pregnancy was normal. He was well until three days before admission to hospital when he was noted to be drowsy and pale, and he vomited several times. Twenty-four hours before admission his breathing became rapid, and grunting and cyanosis developed. During the day he passed five loose stools. Examination showed a pale, slightly cyanosed baby with rapid, regular,

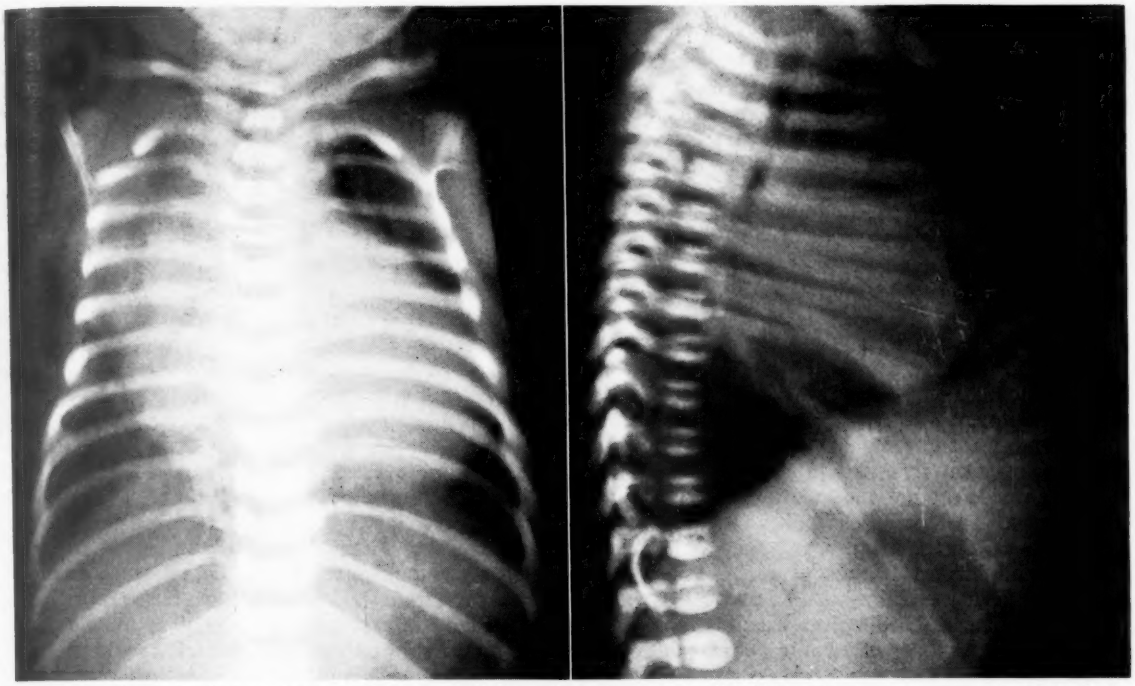


FIG. 2A.—Radiograph of chest showing gross symmetrical cardiac enlargement with slight pulmonary engorgement. Note the low flat diaphragm, the anterior displacement of the sternum and the posterior displacement of the trachea.

slightly grunting, shallow respirations at 60 per minute. The extremities were cold and mottled, the temperature 97° F., and the pulse was weak and thready at 160 per minute. The cardiac size could not be assessed clinically. Heart sounds were regular and faint, and no murmur but gallop rhythm was heard. The chest was barrel-shaped and scattered crepitations were heard over both lung fields. The liver was three fingerbreadths below the costal margin and the tip of the spleen was felt. There was no peripheral oedema, or venous engorgement in the neck. The urine was clear of albumin, cells and casts. A radiograph of the chest showed a grossly enlarged heart, which largely obscured slightly congested lung fields and displaced the trachea and oesophagus posteriorly (Fig. 2A). Digoxin, 0·05 mg. intramuscularly, and oxygen were given, but death occurred four hours later.

Necropsy revealed a symmetrically enlarged, dilated heart, weighing 48 g. The muscle was flabby and appeared mottled with dark and pale areas. The lungs were engorged with some consolidation at the right base and the liver was enlarged and congested (weight, 116 g.). Microscopic examination of the heart showed that the myofibrils had disappeared from extensive areas leaving a reticular structure. Some cellular reaction with lymphocytes, plasma cells and fibroblasts was noted at the periphery of these lesions (Fig. 2B). It appeared that these lesions had been present for a longer time than was indicated by the infant's symptoms.

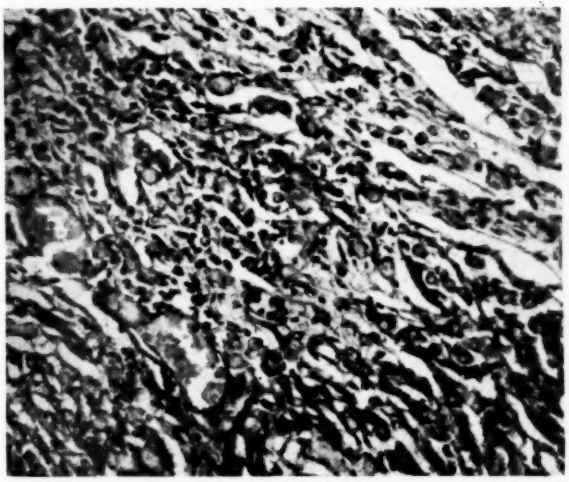


FIG. 2B.—Histological section of the left ventricular wall showing gross muscle cell necrosis and vacuolation with cellular infiltration. ×110.

Case 7. S.A., a boy aged 3 weeks, was admitted to the Children's Hospital on March 4, 1952. He was a normal full term baby of healthy parents and the pregnancy had been normal. He had made good progress until 11 days old when he became off colour and later his breathing was rapid and grunting and his colour greyish. Periodically he screamed and drew up his legs as if in pain. Two days later he temporarily improved but was not well. For the next five days his condition was unchanged but then he developed a cough, and became pale and listless. Later he was cyanosed with rapid, grunting breathing. Examination showed an ill, cyanosed baby with a respiratory rate of 70 per minute, a temperature of 95° F.,

a pulse rate of 160 per minute, cold mottled extremities and poor capillary circulation. The heart was clinically enlarged with pulsation in the fifth left intercostal space outside the nipple line and in the epigastrium under the xiphisternum. The heart sounds were faint but no murmurs were heard. No cervical venous congestion was observed. The chest was slightly emphysematous and scattered crepitations were heard more on the right side than the left. The liver was palpable three fingerbreadths below the costal margin and the tip of the spleen was palpable. No subcutaneous oedema was noted. A radiograph of the chest showed gross uniform cardiac enlargement with mild congestive changes in the lung fields, and a radio-opacity in the right lower lung. A clinical diagnosis of congenital heart disease with congestive cardiac failure and respiratory tract infection was made and treatment with oxygen, penicillin and streptomycin given, but the infant died eight hours later.

Necropsy revealed an enlarged heart (weight, 47 g.) with the right side more dilated than the left, and some small petechial haemorrhages along the line of the coronary vessels. The lungs were congested and oedematous and small bilateral serous pleural effusions were present. The liver was enlarged and congested with a nutmeg appearance. Histological examination of the heart showed patchy areas of myofibril damage throughout the left ventricle and to a lesser extent in the other chambers. The cellular reaction consisted mainly of lymphocytes and polymorphonuclear leucocytes.

Case 8. R.D., a girl aged 15 months, was admitted to the Children's Hospital on March 7, 1952, with a history of malaise and slight fever for one week, and rapid grunting breathing, pallor and cyanosis for four days. The baby had been treated for pneumonia for three days. Examination showed a very ill, restless, pale, slightly cyanosed, apprehensive-looking baby. The respiratory rate was 50 per minute, the chest was barrel-shaped and no crepitations were heard. The extremities were cold and mottled, the capillary circulation very poor, the pulse rate 150 per minute, and the blood pressure 70/50 mm. Hg. Cardiac pulsation was felt in the fifth left intercostal space outside the nipple line, in the third and fourth right intercostal spaces close to the sternum and in the epigastrium. Gallop rhythm and distant heart sounds were heard but no murmur was present. The liver edge was felt four fingerbreadths below the costal margin and the spleen was just palpable. No subcutaneous oedema was detected. There was moderate albuminuria but no cells or casts in the urine. A radiograph of the chest showed gross symmetrical cardiac enlargement, slightly hazy lung fields which were not congested, and small bilateral pleural effusions. The electrocardiogram showed a rate of 150 per minute, low voltage ventricular complexes and isoelectric T waves in all three standard leads. Digoxin, 0·2 mg. statim was given intramuscularly, and 0·2 mg. in six hours together with oxygen. The infant did not improve and died suddenly eight hours after admission.

Necropsy revealed a flabby, enlarged heart (weight, 95 g.) with some oedema of the lungs and moderate enlargement and congestion of the liver. Histologically the heart showed diffusely scattered foci of fragmented and oedematous muscle fibres. Lymphocytes and macrophages infiltrated the entire muscle but were aggregated particularly in and around the foci of muscle damage. The lungs showed diffuse areas of haemorrhage with mononuclear cells and macrophages in the alveoli. The liver was congested with some fat accumulation.

Case 9. J.B., a girl aged 12 days, weighing 5 lb. 12 oz., was admitted to the Children's Hospital on October 8, 1952. The past history was that of a normal pregnancy and delivery, and the baby had sucked well and made satisfactory progress for the first eight days in the maternity hospital. She went home on the ninth day when she refused her feeds and her breathing was noted to be noisy. The following day the skin was cold and slightly mottled. Over the next two days these symptoms persisted and her stools were noted to be greenish-black and loose. On the day of admission the feet and hands

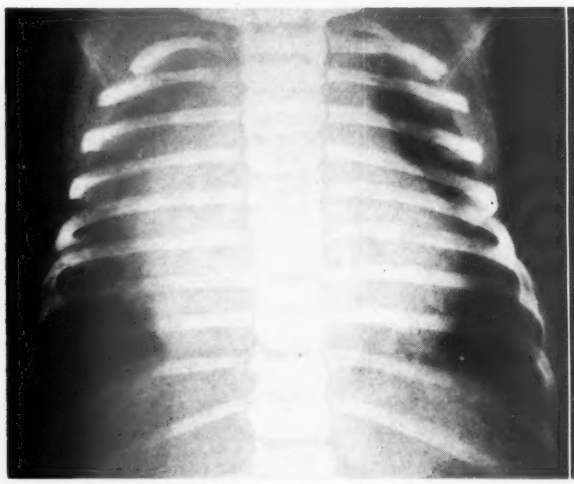


FIG. 3A.—Radiograph of the chest on admission on October 8 showing gross symmetrical cardiac enlargement and slight pulmonary oedema and congestion, and small bilateral pleural effusions.

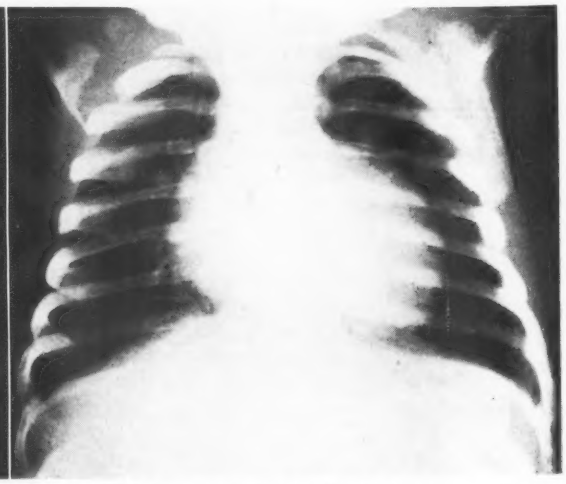


FIG. 3B.—Radiograph on October 24, 16 days later. Normal.

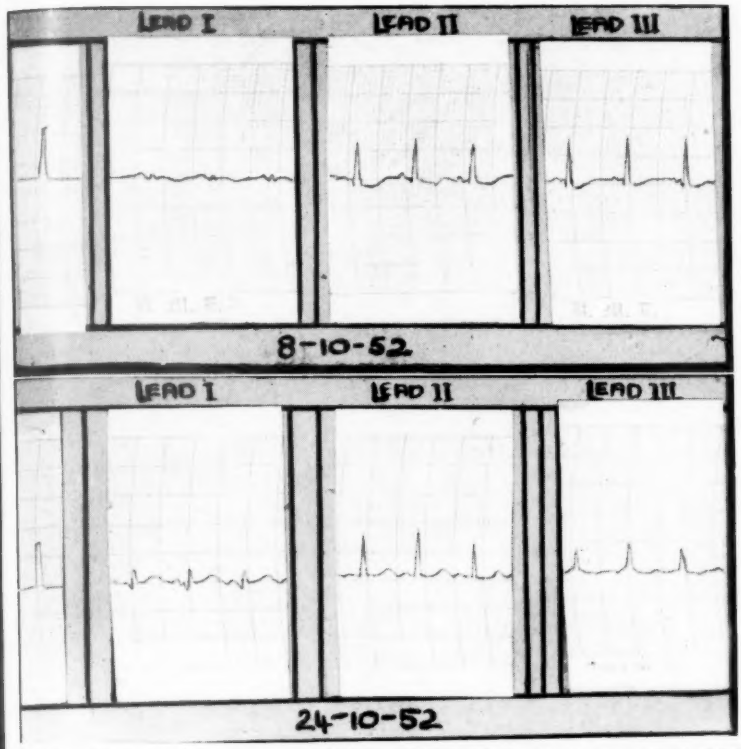


FIG. 3C.—Electrocardiogram on admission on October 8 showing low amplitude QRS complex in lead I and inverted T waves in leads I, II and III.

FIG. 3D.—Electrocardiogram on October 24, 16 days later, upright T waves in leads I and II, increased amplitude of QRS complex in lead I.

became swollen. There was no known contact with infection either in the hospital or at home. Examination showed a small, pale, mottled baby with generalized oedema. The respirations were rapid at 70 to 80 per minute and grunting with some retraction of the lower rib margins. The temperature was 96° F., the pulse rate 150-160 per minute, the extremities cold and the capillary circulation poor. The heart size was difficult to determine clinically but forcible cardiac pulsation was felt in the epigastrium below the xiphisternum. A gallop rhythm but no murmur was heard. The breath sounds were loud and harsh but no crepitations were heard. The liver edge was palpable two finger-breadths below the right costal margin. The urine showed a trace of albumin but microscopically was clear. The cerebrospinal fluid was normal. A radiograph of the chest showed gross symmetrical cardiac enlargement with slight increase in the bronchovascular pattern in the lungs. The electrocardiogram revealed tachycardia of 150 per minute, normal P waves and PR interval, low QRS complexes in all leads, but especially in lead I, and inverted T waves in all leads (Fig. 3A and C).

Digitalis folium, grain ½ statim and grain ¼ six-hourly for four doses and then grain ¼ daily, was administered together with oxygen. After 24 hours' treatment she was much improved. The colour was normal, the respirations easier but still rapid, while the oedema and gallop rhythm were unchanged. The urine was now clear of albumin. In 48 hours the infant had a good cry and sucked well. The liver was now palpable only one fingerbreadth below the right costal margin and the gallop rhythm and oedema had disappeared. Rapid improvement continued and by the sixth day the heart was much smaller radiographically, the pulse rate 130 per minute and respiratory rate 36 per minute. An electrocardiogram showed increased amplitude of the QRS complex with small upright T waves in lead I but there was no other significant change in leads II and III. Improvement was maintained on digitalis and 16 days after treatment began the baby was clinically normal. The heart was normal in size radiologically and the electrocardiogram showed normal T waves in leads I and II but the QRS complex in lead I was still low (Figs. 3B and D). After six weeks' treatment the baby weighed 8½ lb., was clinically normal; the radiograph of the heart was normal and the electrocardiogram showed upright T waves in leads I and II and further increase in the amplitude of the QRS complex in lead I.

Subacute and Chronic Myocarditis

In contrast to the group of nine patients with an acute illness and rapid onset of severe heart failure, five patients had an illness of more gradual and insidious onset before cardiac failure developed. Four of these five patients recovered but all have residual myocardial damage. The prodromal symptoms were those of general malaise or vague ill-health for a month or more before symptoms directly referable to myocardial failure developed. The outstanding and constant symptoms of failure were vomiting, rapid, grunting breathing, pallor, cyanosis and later oedema. The physical signs present in all were cardiac enlargement, tachycardia, gallop rhythm, gross liver enlargement and, by contrast, minimal signs of pulmonary congestion. Radiologically there was gross but symmetrical cardiac enlargement, hazy and slightly congested lung fields and often small bilateral pleural effusions. The electrocardiographic findings were the same as in the acute type. The P waves and PR interval were normal, the amplitude of the QRS complex was low in all leads but especially in lead I, and the T waves were either flat, isoelectric or inverted. The course of the disease was prolonged. All responded to digitalis therapy, but relapsed at varying intervals

following its cessation. All have permanent cardiac damage and in two there is evidence of a mitral valvular lesion. The pathological lesions in the patient who died were essentially the same as those in the acute group. While it is not possible to prove that the pathological lesion in the four survivors was the same, the clinical, radiological and electrocardiographic features were identical.

Case 10. M.H., a girl aged 3 years, weight 34 lb., was admitted to the Children's Hospital on August 4, 1949. One month previously she had contracted an upper respiratory tract infection and had not been well since. Her brother and both parents had also contracted a similar infection. One week before admission she developed abdominal pain, flatulence and vomiting. Distressed breathing, pallor and pain in the chest for one day were the cause of her admission to hospital, She was a pale, cyanosed child with rapid respirations of 50 per minute, and a weak, rapid pulse of 150 per minute. Her temperature was 98° F., and her blood pressure 75/50 mm. Hg. The veins in the neck were engorged and the heart clinically enlarged. The heart sounds were soft, and gallop rhythm but no bruit was heard. The chest was clear clinically, the liver enlarged four fingerbreadths below the costal margin and the sacrum and feet pitted on pressure.

Radiologically the heart was very large and by contrast the lung fields were only slightly congested and hazy. The electrocardiogram showed low QRS complexes and flat T waves in all leads. No pathogenic organisms were cultured from the throat swab and the antistreptolysin titre in the serum was less than 25 units per ml. The urine was normal chemically and microscopically. Treatment with oxygen and digoxin, 1 mg. during the first day, 0·4 mg. during the second day, and then ½ grain digitalis folium daily, produced rapid relief of her symptoms. After one week she was well, the heart rate was 80 per minute, but the heart was still somewhat enlarged. After four weeks on digitalis she was sent home and was well for five weeks when she caught a 'cold', after which she again became off colour, complained of abdominal pain and was short of breath. All the signs of cardiac failure recurred and she was re-admitted to hospital. Again culture of the throat swab yielded no pathogenic organisms and the serum antistreptolysin titre was less than 50 units per ml. Treatment with digitalis again produced a good response, and after one month's treatment she was sent home clinically well but with an enlarged heart. Seven months after the original attack a slightly rough, 'blowing' apical systolic murmur appeared for the first time and this has persisted unchanged to August, 1952. She has been well during this time, enjoys full activity, but her heart is still slightly enlarged both clinically and radiologically. Her electrocardiogram is normal.

Case 11. F.P., a girl aged 20 months (weight 22½ lb.), was admitted to the Children's Hospital on August 29, 1950, with a history of being off colour for one month. One week before admission she began to vomit and passed very little urine. Her face and feet gradually became swollen and her breathing rapid and grunting. She was the only child of healthy parents, had always been well and had not been in contact with any person with an infectious disease. Examination showed an ill, cyanosed infant with rapid, grunting respirations at 60 per minute, a weak, thready pulse of 160 per minute, cold, mottled extremities and a temperature of 99° F. The heart was enlarged clinically, and gallop rhythm but no murmur was heard. The blood pressure was 90/70. The liver edge was felt three and one-half fingerbreadths below the costal margin, crepitations were heard at both lung bases and slight oedema of legs, sacrum, hands and face was noted. The urine contained a trace of albumin, a few red blood cells and an occasional cast for one day, after which it was normal. A radiograph of the chest showed gross symmetrical cardiac enlargement, a small bilateral pleural effusion and a radio-opacity in the right lower zone which was considered to be an area of consolidation (Fig. 4A). The serum antistreptolysin titre was less than 50 units per ml. The electrocardiogram showed a sinus tachycardia of 160 per minute, normal P waves and PR interval, low QRS complexes and isoelectric T waves in all three standard leads (Fig. 4C). Treatment with digitalis folium, grains 4 for 24 hours, grains 2 daily for two days, and then grain ½ daily, together with oxygen, produced a satisfactory response. In 72 hours she was beginning to play. The pulse rate was now 88 per minute, the respirations 30 per minute and the blood pressure 110/86 mm. Hg. The oedema of the face and crepitations in the lungs had cleared, the liver edge was just palpable and she had lost 2 lb. in weight.

Digitalis therapy was discontinued after one month, when the infant was well but the heart still enlarged. Two weeks later following an upper respiratory tract infection all the signs and symptoms of congestive failure recurred and the infant was as ill as previously. On this occasion digitalis therapy did not produce a rapid clinical improvement. After ten days failure was still pronounced and 'mersalyl' injections (0·25 ml. intramuscularly daily) were begun. While this treatment reduced some of the oedema, the heart still remained large, the rate rapid at 120 per minute, and gallop rhythm was intermittently heard. The liver edge remained three fingerbreadths below the costal margin. During the next eight months, despite digitalis folium, grains ¾ daily, and 'mersalyl' 0·5 ml. on alternate days, the infant remained in a state of chronic cardiac failure. Approximately one year after the illness she began to improve slowly, looked better, the heart rate became slower, the heart size smaller and the liver gradually returned to a normal size. A blowing systolic murmur now developed at the apex. In November, 1952, two years and three months after the initial illness, she was very well. The heart was clinically and radiologically still enlarged, and the electrocardiogram showed low T waves in all leads (see Figs. 4B and D).

Case 12. D.B., a girl aged 6 years, was admitted to the Children's Hospital on August 22, 1950, with the history that she had always been well until five weeks previously when she became listless, lost her appetite, developed a slight dry cough and became breathless on

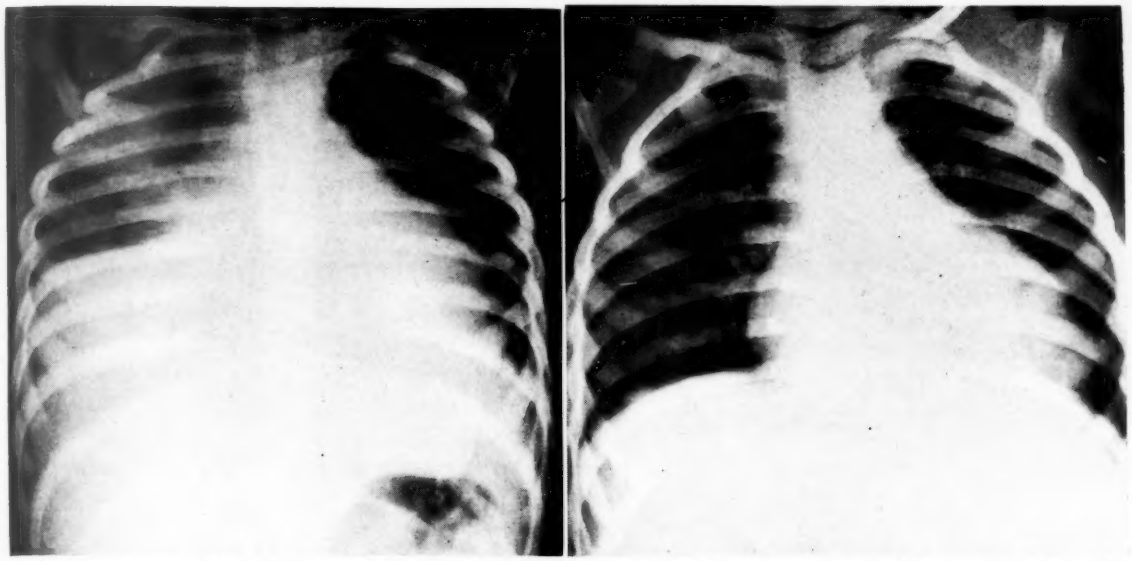


FIG. 4A.—Radiograph of chest on admission on August 20, 1950, showing gross cardiac enlargement, an opacity in the right lower lung field and a small left pleural effusion. The opacity was considered to be the result of a right lower lobe consolidation.

FIG. 4B.—Radiograph of June 17, 1952, showing slight cardiac enlargement. Child clinically well but with evidence of a mitral valve lesion.

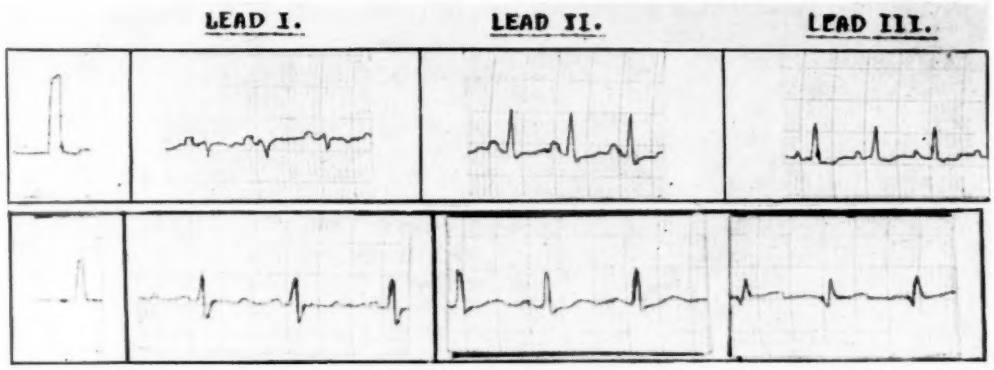


FIG. 4C.—Electrocardiogram on August 20, 1950 (above) showing low amplitude QRS complex in lead I and inverted T waves in leads I, II and III. D.—Electrocardiogram on June 17, 1952 (below) is normal apart from low T waves in all leads.

walking. The parents and three other children were well and the patient had not been in contact with any infectious disease. Examination showed a sick child, with a temperature of 98° F., quiet respirations of 24 per minute, pulse 130 per minute, and a blood pressure of 75/50 mm. Hg. The heart was considerably enlarged clinically and gallop rhythm, but no murmur, was heard. The veins in the neck were engorged, the liver enlarged three fingerbreadths below the costal margin, the lungs were clear but the legs and sacrum pitted on pressure. The urine was clear of albumin and cells. A radiograph of the chest showed a grossly enlarged heart but no pulmonary engorgement. The electrocardiogram showed a tachycardia of 120 per minute, normal P waves, normal PR interval, low voltage QRS complexes and very low T waves in all three standard leads. The serum antistreptolysin titre was below 25 units per ml. and culture of the throat swab did not grow any pathogenic organisms. With digitalis folium, grains 8 over 48 hours and then grain 1 daily, the child rapidly improved so that in three days the heart rate was 80 per minute, the gallop rhythm and subcutaneous oedema had disappeared and the liver edge was palpable only one fingerbreadth below the costal margin. The electrocardiogram showed that the QRS complexes and T waves were returning to normal. During the next six months she remained well while resting in bed, but the heart remained grossly enlarged. At this time she was allowed up but would not attempt to run or hurry as she became very breathless. The heart remained very enlarged and the pulse rate 90 to 100 per minute. After a period of about six months, i.e. approximately one year after she first became

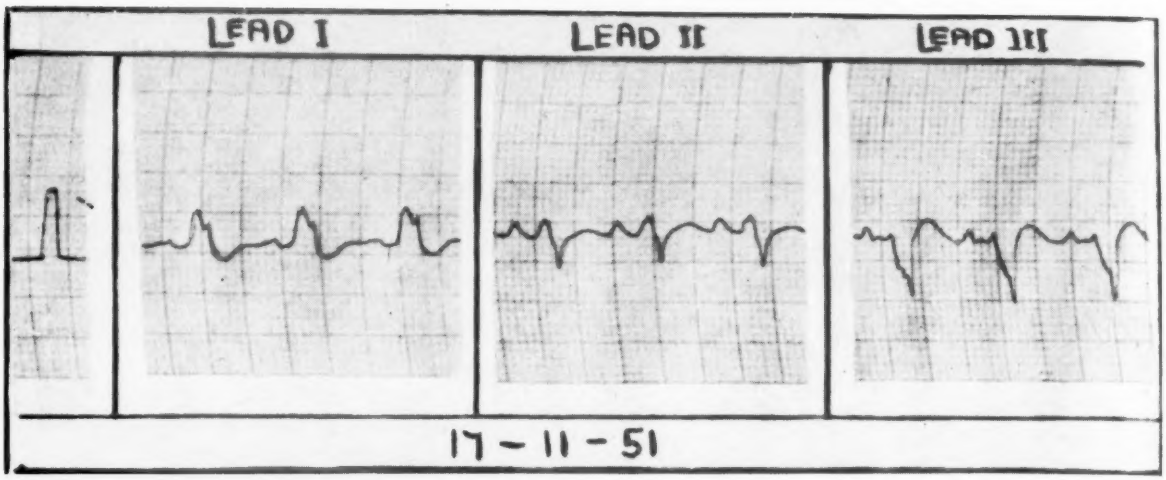


FIG. 5A.—Electrocardiogram showing bundle branch block.

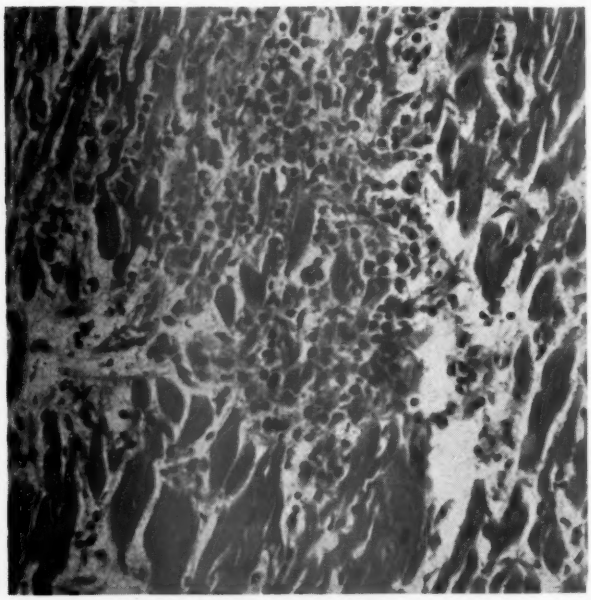


FIG. 5B.—Histological section of ventricular wall showing a patch of muscle cell damage with inflammatory cell reaction. ×110.

ill, congestive cardiac failure again developed. Even with complete bed rest, digitalis and later 'mersalyl' injections a satisfactory response did not occur. The heart rate remained rapid at 120 per minute, the heart grossly enlarged, the legs and sacrum oedematous and the liver grossly enlarged. An electrocardiogram showed an early bundle branch block (Fig. 5A). The congestion gradually became more marked, the subcutaneous oedema increased, a complete bundle branch block developed and the child died 16 months after she first took ill.

Necropsy revealed gross enlargement of the heart due mainly to dilatation of all chambers. The ventricular walls were a little hypertrophied, the right side more than the left. Histologically the muscle cells showed patchy gross vacuolation while scattered areas of round cell infiltration were noted between the muscle fibres (Fig. 5B). The coronary vessels showed slight thickening of the intima. No Aschoff nodules, endocarditis or pericarditis were observed. The lungs were very oedematous with chronic congestive changes and the liver enlarged with a typical nutmeg appearance.

Case 13. R.O., a girl aged 18 months, was admitted to the Children's Hospital on October 13, 1951, with the history that at the age of 5 months she became off colour, developed a nasal discharge and later on a cough and wheeze. As these symptoms persisted it was considered that she might have had a chronic lung infection. Radiological examination of the chest showed that the only abnormal feature was moderate symmetrical cardiac enlargement. From the age of 7 to 18 months she was well, grew and developed normally but serial clinical and radiological examinations showed that the heart was persistently enlarged. At 18 months of age she insidiously became ill and was admitted shortly after with congestive heart failure. She was moderately dyspnoeic with a respiratory rate of 46 per minute, a pulse rate of 150 per minute and temperature of 99° F. The heart was grossly enlarged, and gallop rhythm but no bruit was heard. The veins in the neck were engorged, the liver palpable three and one-half fingerbreadths below the costal margin, scattered rhonchi were heard in the chest and the feet and legs were oedematous. A radiograph of the chest revealed gross symmetrical cardiac enlargement and only slight engorgement and haziness of the lung fields. An electrocardiogram showed a heart rate of 160, normal P waves and PR interval, normal QRS complexes but isoelectric T waves. Treatment with digitalis folium, 7½ grains for three days with 'mersalyl', 0·5 ml. daily, resulted in rapid improvement. The heart rate fell to 80 per minute, the gallop rhythm disappeared, the liver receded to two fingerbreadths and the oedema disappeared. During the next week the child continued to improve. However, the heart remained enlarged, and the liver edge was palpable one fingerbreadth below the

costal margin. Digitalis was discontinued after three weeks but convalescence was interrupted by an intercurrent respiratory tract infection. She was sent home six weeks after admission.

During the next eight months she was not well. Periodic clinical examinations from November, 1951, to July, 1952, showed a moderately enlarged heart, with at times a triple rhythm, and the liver edge was palpable two fingerbreadths below the costal margin. Gradually the congestive failure became worse and she was again admitted to hospital on July 30, 1952, with a grossly enlarged heart and liver. The electrocardiogram showed a tachycardia with isoelectric T waves. Treatment with digitalis produced a very satisfactory response and by November, 1952, the only abnormal findings were a moderately enlarged heart and flat T waves in the electrocardiogram.

Case 14. T.W., a boy aged 17 months, was admitted to the Children's Hospital on August 12, 1952, having progressed normally until nine weeks previously when he became off colour and feverish. No other members of the household were sick. Later he vomited and his breathing became rapid and grunting. His family doctor then made a diagnosis of bronchopneumonia and prescribed sulphonamide tablets. Over the next two weeks he seemed to slowly improve but one week later the vomiting and distressed breathing recurred. Again a diagnosis of bronchopneumonia was made and treatment with penicillin given without improvement. The colour remained poor, the respirations rapid, and one month later the feet, hands and face gradually became swollen and he passed only small quantities of urine. Examination showed a flushed, sick-looking infant with a temperature of 100° F., pulse rate 130 per minute and respirations of 50 per minute, with some retraction of the lower part of the thorax on inspiration. The heart was enlarged clinically, the sounds were distant and gallop rhythm was heard. The veins in the neck were engorged, and the chest was emphysematous with a few crepitations over the right side anteriorly. The liver was enlarged four fingerbreadths below the right costal margin. Generalized oedema, including swelling of the face, was present. A radiograph of the chest showed gross symmetrical enlargement of the heart, with slight congestion and haziness of the lung fields and small bilateral pleural effusions. An electrocardiogram showed normal P waves, and PR interval, almost isoelectric T waves and low voltage QRS complexes. The urine was clear chemically and microscopically. Digitalis folium, grains 6½, was given for 24 hours and then grain ½ daily. Within 48 hours the infant was very much better. The pulse rate was 80 per minute and the respirations were quiet at 20 per minute. The oedema had decreased, the weight had fallen by 2½ lb., and the liver was palpable only one-half fingerbreadths below the costal margin. Rapid and satisfactory progress was maintained so that digitalis was discontinued after 17 days. The electrocardiogram was now normal, the heart very much smaller radiographically, the liver edge just palpable, and all oedema had disappeared. As the child continued to remain well he was allowed to go home six weeks after treatment began, the only abnormal finding being slight cardiac enlargement.

On arrival home he seemed to contract a slight 'cold' which cleared in three days. One week later he became irritable and vomited and then began breathing rapidly and three days later, on September 1, 1952, was readmitted with congestive cardiac failure. The heart was considerably enlarged, gallop rhythm was audible and the liver palpable three fingerbreadths below the right costal margin. The electrocardiogram showed a heart rate of 160 per minute, with low ventricular complexes especially in lead I and isoelectric T waves in all leads. Response to digitalis therapy was prompt and he steadily improved. Eleven weeks later while still on digitalis he was very well, but the heart was still moderately enlarged and the electrocardiogram still showed rather low QRS complexes but normal T waves.

Discussion

Aetiology. The aetiology of the myocarditis in this group of children is unknown. The role that infection plays is uncertain and on the available evidence impossible to decide. Clinically three of the 14 patients had a mild associated respiratory tract infection and one other of those who died had post-mortem evidence of pneumonia. While detailed bacteriological and virus investigation was not conducted either during life or after death, 10 of the 14 patients had neither clinical nor pathological evidence of infection, and interrogation failed to determine a contact source of infection.

Identical myocardial lesions have been found associated with many different infections and Saphir with his co-workers give a full review in a series of papers (Saphir, 1941, 1942; Saphir and Wile, 1942; Saphir, Wile and Reingold, 1944; Gore and Saphir, 1947). In infancy and childhood the infections most commonly associated with myocarditis are diphtheria, poliomyelitis and measles, but myocarditis has been found occasionally with almost every infection. The similarity of the pathological lesions in our patients to those described with a known infection suggests, but does not establish, an infective aetiological basis.

It might be considered that the four patients with subacute myocarditis who recovered, and especially the two who developed an apical systolic bruit, did not have idiopathic but rheumatic myocarditis. Such a diagnosis is highly improbable on the grounds of the very young age of the patients, the complete lack of other clinical manifestations of rheumatic infection and the absence of both pericarditis and endocarditis during the active phases of the disease when congestive failure was present. In addition the electrocardiographic changes with grossly abnormal T waves and low amplitude

ventricular complexes, and the repeatedly low antistreptolysin titres recorded in the serum are features which are rarely encountered in rheumatic carditis.

Pathology. The constant features seen on histological examination were widespread but patchy necrosis and fragmentation of muscle fibres, and a cellular reaction. Some of these foci of cellular aggregations had an oedematous appearance. The cell type was not constant; neutrophil and eosinophil polymorphonuclear leucocytes, lymphocytes, plasma cells, and macrophages varied in their relative proportions and in one case fibroblast proliferation was present. No correlation was possible between the duration of illness and apparent age of the lesion as judged by the histological pattern. These changes were in no way different from those encountered in myocarditis occurring in infectious diseases.

Kugel and Stoloff (1933) and Kugel (1939) have described a syndrome in infants and young children of cardiac failure due to a non-suppurating myocardial degeneration with cardiac dilatation and hypertrophy. The clinical features of this syndrome closely resemble those of some of our own patients. However, the morbid anatomical changes are different and consist of a very dilated hypertrophied heart with foci of atrophied and degenerated muscle fibres with fibrosis. Occasionally there is a cellular reaction with a few lymphocytes. The relation of these pathological changes to those occurring in idiopathic myocarditis cannot be decided, but they may represent a late stage of idiopathic myocarditis.

Clinical Features. This group of patients demonstrates that idiopathic myocarditis is of variable severity. The lesion may either kill rapidly, resolve completely, or leave residual heart damage. It has been established that myocarditis may cause sudden and unexpected death in infancy (Bowden, 1950), while in others heart failure occurs which may result in death or partial or complete recovery. However, it it is likely that there are mild grades of the disorder which do not cause heart failure and which are unrecognized clinically. Neubauer (1944), Lyon (1947) and others have shown that myocarditis of varying degrees of severity is common in a wide variety of infectious diseases and that death occurs only in the more severe lesions. Pallor, malaise, tachycardia, abnormalities in the quality of the heart sounds and also in the electrocardiogram may be the only manifestations of the disease in the milder cases.

There are two main reasons why myocarditis is rarely diagnosed clinically. First, it is generally believed to be a very uncommon disorder and therefore is rarely considered. Second, the pattern of acute cardiac failure in a young infant can be a confusing one unless encountered previously. Distressed, rapid breathing, cyanosis, cold extremities, poor capillary circulation and tachycardia occur in both cardiac failure and severe acute respiratory tract infections, especially pneumonia. Failure to demonstrate cardiac enlargement is the most important reason for mistaking acute heart failure for pneumonia. It is often impossible in a restless infant with a respiratory rate of 50 to 100 per minute to determine the size of the heart clinically, and in such a patient radiological examination is necessary. Other features such as low or normal temperature with tachycardia, poor quality heart sounds and gallop rhythm, and especially a liver edge palpable three to four fingerbreadths below the costal margin, point to cardiac failure and not pneumonia. It is to be remembered that acute severe bronchiolitis with obstructive emphysema may cause rapid breathing, cyanosis and downward displacement of the liver. The displaced liver in such a patient may easily be mistaken for an enlarged liver.

Paroxysmal tachycardia often gives rise to heart failure if the heart rate is very rapid, and the attack is of some days or weeks' duration. The chief features differentiating the two conditions are the heart rate and alteration in the ventricular complexes and T waves. In myocarditis the rate is rarely above 160 to 170 per minute, while in paroxysmal tachycardia with cardiac failure in infants it is rarely below 200 per minute (Nadas, Daeschner, Roth and Blumenthal, 1952). An electrocardiogram will usually establish the diagnosis but it must be remembered that Lind and Hultquist (1949) have shown that myocarditis may precipitate an attack of paroxysmal tachycardia.

Respiratory distress, cyanosis, and cardiac enlargement in a very young infant may be attributed to heart failure due to a congenital malformation of the heart. The heart failure may have been precipitated by a respiratory tract infection. Differentiation from heart failure due to myocarditis may be difficult but the following points help to establish the diagnosis. The infant with malformation of the heart usually does not thrive, often has mild attacks of cyanosis, and may be found to have an enlarged heart and murmur some time before cardiac failure develops. In contrast to myocarditis pulmonary engorgement is usually gross, the liver not as large, the heart sounds usually louder and often a murmur is present. Gallop rhythm is rarely heard and the electrocardiographic changes rarely show evidence of gross myocardial damage.

Treatment. Infants with cardiac failure from myocarditis are dangerously ill and gentle nursing and minimal handling are essential. No attempt

should be made to feed them until congestive failure is relieved and they should be left undisturbed in a warm cot or bassinette in an atmosphere of oxygen. Even minimal handling may lessen the chance of recovery, therefore cooperation and understanding by the nurse in charge of the infant is essential.

The patient should be rapidly brought under control with digitalis. Two patients in the acute group and all in the subacute group responded promptly to the drug so that within 24 hours there was very appreciable improvement, and by 72 hours most of the signs of failure had disappeared. The dose used has been grain $\frac{1}{4}$ to grain $\frac{1}{5}$ of digitalis folium per pound of body weight, or 0·04 of a milligramme of digoxin per pound of body weight over a period of 24 hours. One-third of the total dose may be given immediately and the remainder in three evenly divided doses, at six-hourly intervals. While a few patients were treated satisfactorily with digitalis by mouth during the first 24 hours, it is wiser to use digoxin intramuscularly to obtain a more rapid effect. Oral therapy seems quite satisfactory after the first 24 hours. Digitalis should be continued with a maintenance dose of approximately grain $\frac{1}{40}$ of digitalis folium per pound of body weight until the heart has returned to a normal size or the cardiac lesion healed. It is difficult to decide when healing has taken place, and as cardiac failure in all patients in the subacute group recurred after cessation of several weeks' treatment, it seems advisable to continue digitalis for a minimum period of three months or longer.

Antibiotic drugs were administered to some patients. There was no evidence that either penicillin alone or in combination with streptomycin or aureomycin alone altered the course of the illness.

Prognosis. The prognosis for the infant or child with a short history and severe circulatory failure was poor. The majority did not respond to digitalis therapy and were dead in less than 24 hours from the beginning of treatment. However, two seriously ill patients recovered completely and it is possible that earlier diagnosis and treatment may aid in the recovery of more patients in this group. All patients with the subacute type of illness made a satisfactory initial response to digitalis, four of them survived but have enlarged hearts and two have a mitral valve lesion. The development of a valve lesion was not surprising as one patient who died had infiltration of the atrioventricular ring and the base of the mitral valve with inflammatory cells. The two patients with a valve lesion have been observed for over two and three years respectively, both are in good health and the cardiac lesion seems stationary. Observation over years will be necessary to learn what will happen to these patients. It is possible that young adults with cardiac enlargement of unknown aetiology and with varying degrees of impaired cardiac function developed their disease in infancy or early childhood, and that it is similar in type to the disease in these patients.

Summary

Idiopathic myocarditis is a serious, frequently fatal malady occurring usually in the first two years of life.

The pathological lesion consists of widespread but usually patchy muscle damage with an associated inflammatory cell reaction.

The common clinical illness is a rapidly developing, usually fatal cardiac failure which is manifested by severe respiratory embarrassment, cyanosis, tachycardia with low or normal temperature, an enlarged heart and liver, and electrocardiographic changes of myocardial damage.

The illness in some patients may be more insidious in onset and the heart failure not as severe. Recovery frequently occurs after a long illness but there is permanent myocardial damage.

The acute form of the disorder is commonly mistaken for pneumonia as respiratory embarrassment and cyanosis are the outstanding clinical features, and cardiac enlargement is difficult and frequently impossible to detect clinically.

Treatment with digitalis and oxygen has been of very definite value in some patients.

The clinical and pathological evidence gives no clue as to the aetiology.

We wish to thank Dr. I. Epstein and Dr. C. Sawrey of the Hamilton Base Hospital for permission to publish cases Nos. 3 and 5, and the Honorary Medical Staff of the Children's Hospital for cases 4, 7, 9, 12 and 13. Dr. H. G. Hiller has kindly reported on the electrocardiograms. Mr. Murphy, Photographic Department, Children's Hospital and Mr. Matthie, Melbourne University, are responsible for the photographs.

References

Bowden, K. M. (1950). *Med. J. Aust.*, **2**, 397.
Gore, I. and Saphir, O. (1947). *Amer. Heart J.*, **34**, 827.
Greenebaum, J. B., Felson, W. and Zeligs, M. (1941). *J. Pediat.*, **18**, 799.
Keller, H. (1945). *Helv. paediat. Acta*, **1**, 57.
Kenny, F. E. and Sanes, S. (1933). *J. Pediat.*, **3**, 321.
Kugel, M. A. (1939). *Amer. Heart J.*, **17**, 602.
—— and Stoloff, E. G. (1933). *Amer. J. Dis. Child.*, **45**, 829.
Lind, J. and Hultquist, G. T. (1949). *Amer. Heart. J.*, **38**, 123.
Lyon, E. (1947). *Med. Rec., N.Y.*, **160**, 402.
Maslow, H. L. and Lederer, M. (1933). *Amer. J. Dis. Child.*, **45**, 807.
Nadas, A. S., Daeschner, C. W., Roth, A. and Blumenthal, S. L. (1952). *Pediatrics*, **9**, 167.
Neubauer, C. (1944). *Archives of Disease in Childhood*, **19**, 178.
Saphir, O. (1941). *Arch. Path., Chicago*, **32**, 1000.
—— (1942). *Ibid.*, **33**, 88.
—— and Wile, S. A. (1942). *Amer. J. med. Sci.*, **203**, 781.
—— —— and Reingold, I. M. (1944). *Amer. J. Dis. Child.*, **67**, 294.
Scott, R. W. and Saphir, O. (1929). *Amer. Heart J.*, **5**, 129.
Smith, F. M. and Stephens, R. L. (1938). *Trans. Ass. Amer. Phys.*, **53**, 120.

LEFT AURICULAR ENLARGEMENT IN ENDOCARDIAL FIBRO-ELASTOSIS

BY

J. L. FREER and W. J. MATHESON

From the Radiological Department and Children's Hospital, Leicester Royal Infirmary

(RECEIVED FOR PUBLICATION APRIL 27, 1953)

Endocardial fibro-elastosis or endocardial sclerosis, a disease in which the endocardium, mainly of the left side of the heart, is greatly thickened with fibrous and elastic tissue, is now being more frequently recognized. In 1946 Cosgrove and Kaump collected 44 cases from the literature and added six of their own. Since then at least an equal number of cases has been reported, including a description of 25 by Blumberg and Lyon (1952) collected over a period of five years.

The majority of cases occur in infancy: they present with signs of heart failure either of sudden onset and rapidly fatal, or running a more prolonged course fluctuating in severity but in the end also causing death. The other outstanding clinical feature is cardiac enlargement, usually gross and usually unaccompanied by cardiac murmurs.

A presumptive diagnosis can certainly be made on clinical grounds alone, but we have found that the radiological demonstration of left auricular enlargement is a useful confirmatory sign.

Case Reports

Case 1. A girl aged 6 years was admitted to hospital in cardiac failure. On examination the heart was grossly enlarged; there was a faint apical systolic murmur. Radiographs showed marked cardiac enlargement, mainly of the left auricle and ventricle. Thought to be suffering from acute rheumatism, she improved for a time with salicylates and digitalis but died suddenly a week after admission. Post-mortem examination confirmed the cardiac enlargement mainly affecting the left side; the endocardium was not considered to be abnormal macroscopically but sections showed marked endocardial thickening.

Case 2. A girl aged 2 years was admitted to hospital in cardiac failure. On examination the heart was greatly enlarged. Radiographs showed left auricular enlargement (Fig. 1 and Table 1). Although she improved initially, there was persistent tachycardia with apical triple rhythm, heart failure recurred, and she died two months after admission. Necropsy confirmed the cardiac enlargement affecting mainly the left auricle and ventricle (Fig. 2); the endocardium was white and thickened on section and this thickening was shown to be mainly due to an increase in elastic fibres (Fig. 3).

Case 3. A girl aged 3 years was admitted because of abdominal distension of one month's duration and

TABLE 1
SUMMARY OF CARDIAC AND PULMONARY CHANGES IN PRESENT SERIES

Case No.	Cardiac Enlargement	L. Auricle (P.A. View)	L. Auricle (R.A.O.)	Pulmonary Changes
1	+++	0	++	++
2	+++	++	+++	+
3	+++	++	not obtained	++
4	++	+	+	++
5	+++	0	++	++
6	+++	+	+++	+++
7	++	0	++	+++

+ = Minimal changes, ++ = definite changes, +++ = marked changes.

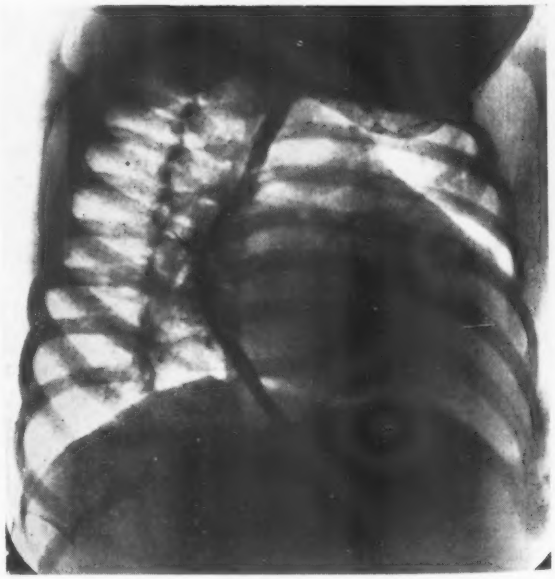


FIG. 1.—Case 2. R.A.O. view showing left auricular enlargement.

FIG. 2.—Case 2: heart showing left ventricle which is much enlarged; towards the apex the endocardium is white and thickened.

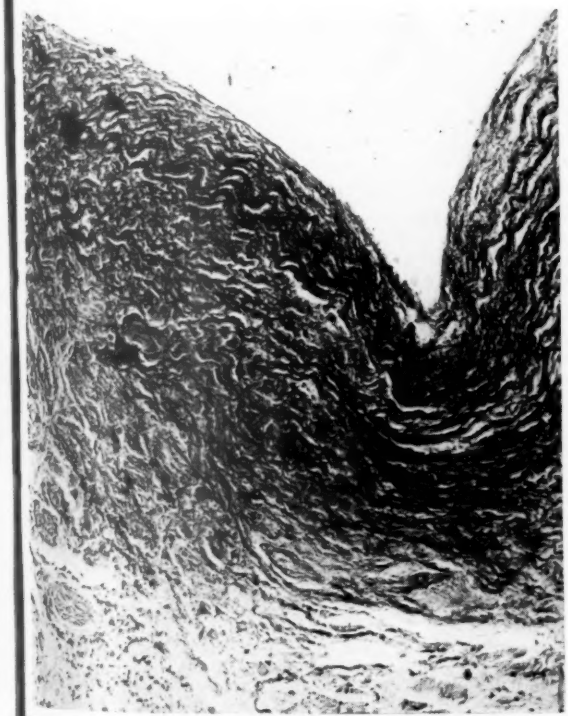


FIG. 3.—Case 2.—Section of left auricle (Weigert's elastin stain ×210) showing thickening of endocardium and great increase of elastic tissue.

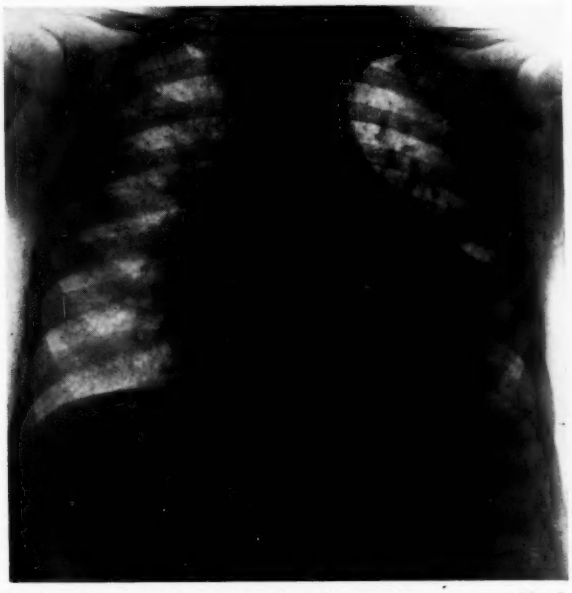


FIG. 4.—Case 3. P.A. view showing left auricular shadow within the cardiac shadow.

FIG. 5.—Case 4. P.A. view showing oesophageal displacement to the right.

swelling of the legs and eyelids for one week. She was thought to have a primary abdominal sarcoma with extension to the mediastinum. Radiographs, however, showed marked cardiac enlargement and enlargement of the left auricle in the postero-anterior view (Fig. 4 and Table 1). There was persistent dyspnoea and tachycardia and she died after a month in hospital. Post-mortem examination showed gross dilatation of the left auricle and ventricle; the endocardium was thickened and the liver cirrhotic.

Case 4. A girl was aged 14 months on first admission to hospital because of wheezing, difficulty in swallowing solids, and abdominal enlargement of four months' duration. Physical examination showed enlargement of the liver, spleen and lymph nodes. She was thought to be suffering from a form of reticulosis and was discharged after one month in hospital, her symptoms having disappeared. Readmitted a month later, she was obviously in cardiac failure which persisted despite digitalization. Terminally she developed a pleural effusion. Radiographs showed cardiac enlargement with displacement of the barium-filled oesophagus to the right in the postero-anterior view (Fig. 5 and Table 1). Necropsy confirmed the cardiac enlargement mainly affecting the left side; the endocardium was thickened and there was a mild degree of mitral stenosis. Histological examination showed that the endocardial thickening was due mainly to a great increase in elastic fibres (Fig. 6).

Case 5. A girl was aged 2 weeks when first seen because of cyanotic attacks. The heart was enlarged and she was in cardiac failure. She improved for a time with digitalis although the cyanotic attacks continued, but died at the age of 8 weeks. Radiographs showed gross cardiac enlargement with marked enlargement of the left auricle

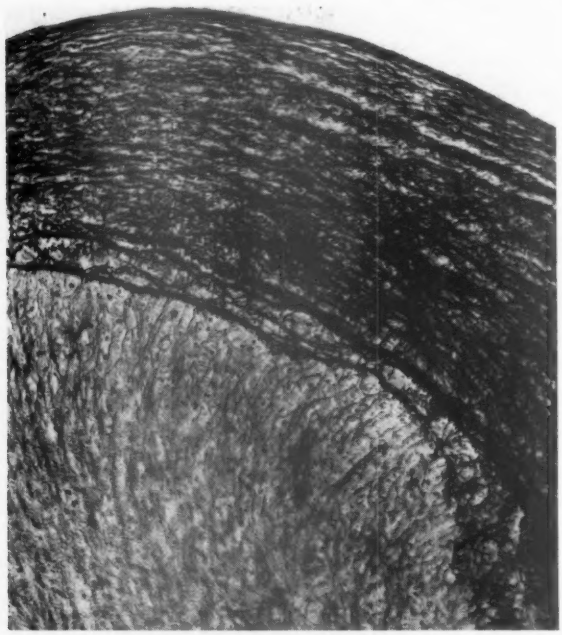


FIG. 6.—Case 4: section of left auricle (Weigert's elastin stain ×90) showing the increase of elastic tissue in the endocardium.

FIG. 7.—Case 6. R.A.O. view showing left auricular enlargement.

(Table 1). Post-mortem examination confirmed the cardiac enlargement; only the endocardium of the left auricle was thickened.

Case 6. A girl was aged 14 months on first admission to hospital. The history was of intermittent pyrexia and changing signs in the chest for the past month. The heart was grossly enlarged, there were signs of infarction at the right lung base, and the child was in cardiac failure. There was rapid improvement with digitalis and she was discharged after one month in hospital. Radiographs showed marked cardiac enlargement and marked enlargement of the left auricle (Fig. 7 and Table 1). She was readmitted a month later with signs of pulmonary infarction which soon cleared, and again six weeks afterwards when she died of cardiac failure a few hours after admission. At necropsy the heart was greatly enlarged, especially the left side where the endocardium was white and thickened.

Case 7. A girl, aged 9 months, was admitted in cardiac failure with a grossly enlarged heart and apical systolic and diastolic murmurs. She did not respond to treatment and died six days after admission. Radiographs showed left auricular enlargement (Table 1). Post-mortem examination showed a large left auricle and left ventricle; there was severe mitral stenosis, the aortic cusps were thickened, and the endocardium was opaque and thickened.

Discussion

Our attention was first drawn to the usefulness of left auricular enlargement as a diagnostic sign when it enabled us to make a retrospective diagnosis in Case 1; here the finding of left auricular enlargement

was unexpected clinically and unexplained at necropsy. When, however, this sign was found also in Case 2 in which a presumptive diagnosis of endocardial fibro-elastosis had been made during life and when this diagnosis was proved at necropsy, the sections of Case 1 were re-examined and the endocardial thickening was then plainly seen. It may be remarked here that the endocardium, classically described as being opaque, white, and glistening, may not appear convincingly abnormal macroscopically at necropsy and sections may be needed to demonstrate the endocardial thickening.

The diagnosis of left auricular enlargement has been based on evidence of backward displacement of the barium-filled oesophagus in the right anterior oblique position, the presence of a dense left auricular shadow within the cardiac shadow in the postero-anterior view and deviation of the barium-filled oesophagus to the right in the postero-anterior position. Fluoroscopy was carried out in six patients, definite left auricular enlargement being present in five (Cases 1, 2, 5, 6, 7); in the other case (Case 4), this enlargement was minimal but additional evidence of it was shown by oesophageal displacement to the right in the postero-anterior view. Radiographs in the right antero-oblique position were obtained in five patients (Cases 2, 4, 5, 6, 7) and confirmed the appearances seen on fluoroscopy. An enlarged left auricular shadow was thought to be demonstrated in the postero-anterior view in two patients (Cases 2 and 3) and in the one case (Case 3) without fluoroscopy or oblique view this was a marked feature.

The other radiological features consisted of cardiac enlargement and pulmonary changes. There was obvious cardiac enlargement in the erect postero-anterior views in every case and the enlargement was considered to be mainly left sided. As regards the pulmonary changes, hyperaemia was present in varying degree in all cases. In two (Cases 4 and 6) there was a suspicion of infarction; Case 4 developed a pleural effusion terminally.

Radiologically the outstanding feature of endocardial fibro-elastosis is that the cardiac enlargement is predominantly left sided in contrast to other congenital abnormalities in which the enlargement is right sided. It is not suggested that left auricular enlargement only occurs in this disease but that its finding, taken in conjunction with the clinical picture, is a useful confirmatory sign. It is realized that backward displacement of the oesophagus may occur with general cardiac enlargement and also that in infants and children the left auricular impression on the barium-filled oesophagus in the right antero-oblique position is more plainly seen than in adults (Evans, 1952). In all our seven cases, however, there was convincing radiological evidence of left auricular enlargement.

Glycogen disease of the heart, which is a much rarer condition, may be impossible to distinguish in life from endocardial fibro-elastosis. It is likely that left auricular enlargement would also be found in glycogen disease although we have not been able to find any reports of this; this enlargement would, however, be part of a general cardiac enlargement not predominantly left sided. In other conditions causing cardiac enlargement in early life left auricular enlargement is not found. Some, like persistent truncus arteriosus and transposition of the great vessels, can be differentiated by the presence of persistent cyanosis while in cases of abnormal origin of a coronary artery an electrocardiogram will show the characteristic T wave changes. Congenital mitral stenosis is usually, if not always, due to endocardial fibro-elastosis, the thickened endocardium distorting the valve; according to Gross (1941) endocardial thickening is found in 70% of cases of so-called foetal endocarditis. Mitral stenosis was found in two of our patients at necropsy (Cases 4 and 7). There was no correlation between its presence and the size of the left auricle as seen radiologically; in fact in Case 4 the left auricular enlargement was considered to be minimal (Table 1).

Blumberg and Lyon's statement (1952) that endocardial fibro-elastosis is one of the commonest types of fatal heart disease affecting infants has been borne out in our experience. The seven fatal cases described here have been seen in a period of 18 months. We have seen in addition three other patients, who are still alive, in whom the clinical picture is typical of this disease; radiographs show marked cardiac enlargement with demonstrable enlargement of the left auricle.

The recognition of the disease is important from a prognostic point of view and we have found the demonstration of left auricular enlargement to be a helpful sign in diagnosis.

Summary

Seven fatal cases of endocardial fibro-elastosis are briefly described. In all left auricular enlargement was demonstrated radiologically and this is considered to be a useful confirmatory sign in diagnosis.

We wish to thank Dr. J. Vernon Braithwaite for permission to record Case 7, and Mr. E. V. Willmott for the photomicrographs.

REFERENCES

Blumberg, R. W. and Lyon, R. A. (1952). *Amer. J. Dis. Child.*, **84**, 291.

Cosgrove, G. E. and Kaump, D. H. (1946). *Amer. J. clin. Path.*, **16**, 322.

Evans, W. (1952). *Cardioscopy*. London.

Gross, P. (1941). *Arch. Path., Chicago*, **31**, 163.

ACUTE ISOLATED MYOCARDITIS IN NEWBORN INFANTS

BY

J. M. DRENNAN

From the Department of Pathology, the Queen's University of Belfast

(RECEIVED FOR PUBLICATION APRIL 30, 1953)

Under such names as isolated myocarditis (Sellentin, 1904), Fiedler's myocarditis (Fiedler, 1899), and myocarditis perniciosa (Boikan, 1931), a rare myocardial disorder of unknown origin has been described which is characterized by progressive heart failure ending fatally after a course lasting weeks or months. In still rarer cases the duration of the illness is measured in days or hours. No age period is exempt from either form of the disease but the fulminating variety is perhaps commoner in young patients. Three cases occurring as early as the neonatal period have already been described. One was an infant aged 6 months (Singer, 1932), the others were newborn babies 9 and 5 days old respectively (Lind and Hultquist, 1949). To this small group the present report adds two other cases. Case 1, a boy, aged 4 weeks, was seen in October, 1950, and case 2, also a boy and aged 1 week, was seen a year later in October, 1951.

Because these young patients succumbed so quickly to the disease an unusually early type of myocardial lesion was preserved for examination. Particular interest therefore attaches to the histological findings in the cases described below.

Case Reports

Case 1. The patient was the sixth child of healthy parents. Two siblings died in infancy of bronchopneumonia following measles, the other three are healthy. There had been no illness in the household during the pregnancy and the child's life. The child was born in hospital and the delivery and puerperium were normal.

He remained perfectly well for four weeks and then developed a slight cough, became irritable and refused food. Twenty-four hours later he was admitted to hospital seriously ill. The face was slightly cyanosed, the respirations increased, the pulse was rapid but the temperature was normal. Lumbar puncture was done because of a bulging fontanelle but the cerebrospinal fluid was clear, not under pressure, and showed no increase in cells. Nothing further was found on general examination. Treatment with oxygen, penicillin and streptomycin produced no improvement and death occurred suddenly a few hours later. The antibiotic treatment comprised two injections of penicillin each of 50,000 units and two of streptomycin each of 0·5 g.

Case 2. This child also happened to be the sixth member of his family. The parents are healthy and all the siblings alive and well. The pregnancy had been uneventful and the child was born at home after a normal labour. He fed well from the bottle and gave no sign of illness until the evening of the seventh day. The onset was then abrupt and the symptoms developed rapidly. The child seemed perfectly well when put into his cot after being fed at 10.30 p.m. but in a few minutes the mother noticed that the face and lips were bluish. When seen by the doctor shortly afterwards the child was pale and apathetic, and on admission to hospital he was in a seriously collapsed condition. The skin was cold and clammy, the respirations gasping. There was some blood and froth on the lips but no sign of injury in the mouth. Coramine was given by injection and the child was immediately removed to an oxygen tent and treated with penicillin and aureomycin. The clinical course was steadily downhill and the child died suddenly after an illness lasting only about 12 hours.

Penicillin was given in an initial dose of 100,000 units followed in six hours by another injection of 50,000 units. Aureomycin, 375 mg., was also given while the child was in hospital.

Necropsy Reports

The two cases were so alike that they may be described together. Both children were normally developed and showed no external evidence of disease, injury or congenital deformity. The lungs were oedematous and congested; a few petechial haemorrhages were scattered over the pleura and the cut surfaces. The hearts were similar in both cases; neither was enlarged or showed any pathological changes whatsoever when opened and dissected. There was nothing of note in the other organs.

Histology. Only the heart need be described. In the routine sections, cut through the anterior walls of the left atrium and ventricle and the anterior cusp of the mitral valve, there were multiple foci of muscle damage and cellular infiltration, which were very much alike in size and distribution in both

FIG. 1.—Earliest stage in the development of the lesion. Muscle striation is replaced by vividly eosinophilic hyaline granules and proliferation of muscle nuclei. (Kull's stain ×650.)

FIG. 2.—Later stage of the lesion showing myocardial degeneration, and muscle fibres filled with brownish-grey amorphous debris and degeneration of proliferated muscle nuclei. At the bottom may be seen longitudinal striations still visible in almost unaffected fibres. (Kull's stain ×650.)

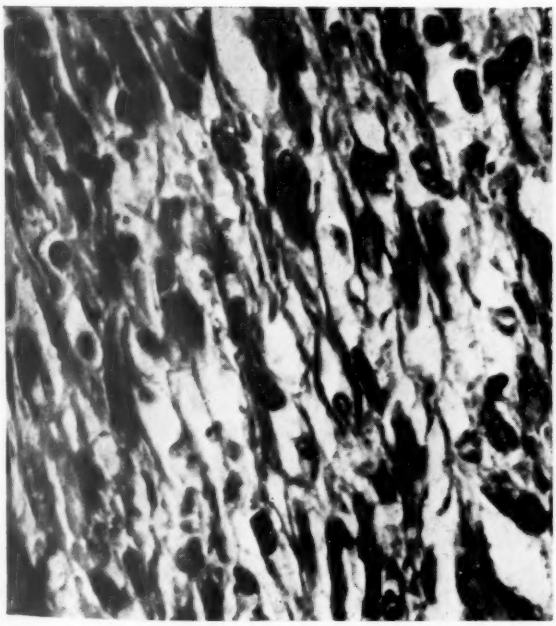


FIG. 3.—End stage of the lesion showing fenestrated appearance due to loss of sarcoplasm. (Kull's stain ×650.)

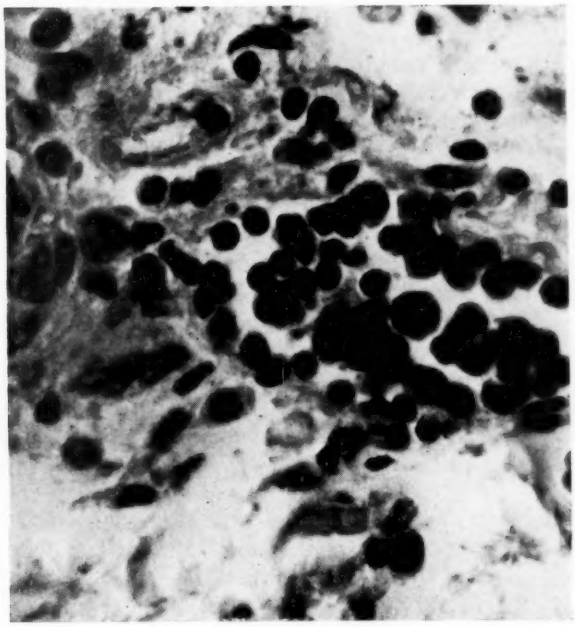


FIG. 4.—Perivascular lymphatic full of macrophages. (Kull's stain ×650.)

hearts. The largest occupied the whole strip of atrial wall in the section, the others, minute, were scattered throughout the ventricular myocardium. Differences in the cellular elements and in the fine detail of the muscle changes as seen in sections stained by a modified Kull's method (Millar, 1933) enabled the lesions to be arranged in a graded series.

In the most acute type of lesion (Fig. 1) the muscle fibres were swollen and crowded with large, intensely eosinophilic hyaline granules: no trace of normal striated sarcoplasm remained. The spaces between the fibres were occupied by proliferated muscle nuclei, but no adventitious cells were present. Lesions presumably of slightly longer standing (Fig. 2) showed progressive degeneration in the sarcoplasm and muscle nuclei, as well as infiltration by adventitious cells. The vividly red granules of altered sarcoplasm seen in the earlier lesions gave place to a brownish amorphous material; the muscle nuclei became shrunken, pyknotic or fragmented; mononuclears, eosinophils and lymphocytes began to appear between the fibres. The end of the process was seen in lesions from which sarcoplasm, muscle nuclei and all but a few inflammatory cells had disappeared, the loss of material giving a fenestrated appearance to the area (Fig. 3).

The epicardium, particularly in Case 1, was diffusely infiltrated by large mononuclears, eosinophils and lymphocytes and these cells also formed nodular collections in the adventitia of some of the arterioles. In the dilated lymphatics of the epicardium, again particularly in Case 1, clumps of large mononuclear cells, some containing ingested eosinophilic material, were often seen (Fig. 4).

Endocardial changes were limited to a slight proliferation of the lining cells wherever a myocardial lesion approached the surface. The valve cusps were not affected.

The essential pathological process was a degenerative change limited to the sarcoplasm of individual muscle fibres, the unaffected nuclei being free to proliferate, at least in the early stages. The degenerate sarcoplasm was rapidly removed by dissolution and phagocytosis, leaving empty spaces to mark the sites of the lesions. Inflammatory cells were absent from the lesions until the degenerative change was well advanced; thereafter mononuclears, eosinophils and lymphocytes appeared in succession. The character of the cellular infiltration and its relation to the muscle lesions showed that it was a secondary reactive phenomenon. The clinical circumstances and necropsy findings served to exclude all the usual causes of myocarditis and failed to reveal any primary disease in organs other than the heart. These cases therefore satisfy the criteria for the diagnosis of isolated myocarditis (Saphir, Wile and Reingold, 1944).

Discussion

Cases of isolated myocarditis surviving for the usual time generally show conspicuous changes in the interstitial tissues of the heart. In a small minority the cardiac muscle is chiefly affected (Gouley, McMillan and Bellet, 1937; Biggart, 1950). The rare cases dying early in the disease are more evenly divided between interstitial and parenchymatous forms. Of the three such cases which have been reported in newborn infants one (Singer, 1932) showed myocardial degeneration, the others (Lind and Hultquist, 1949) interstitial changes only; two adult cases described by Lemke (1924) provided one example of each type of lesion, while that mentioned by Saphir *et al.* (1944) was of the interstitial type.

The classification of isolated myocarditis into a variety of histological types is best regarded at the present time as a descriptive convenience. There is nothing as yet to show that the histological differences correspond to separate disease processes. In fact, the cases described here provide suggestive evidence that some apparently unrelated histological changes may be linked together in the development of a single lesion. On the basis of the present findings the following conclusions seem therefore to be justified in these cases. The primary lesion was a rapidly resolving degeneration of unusual type in the cardiac muscle; it was associated with a cellular infiltration of the interstitial tissue which because of its slower tempo would probably persist after the muscle lesion subsided. Longer survival would therefore have meant a reversal of the histological picture from parenchymatous to interstitial myocarditis so that the cases might have been classified under either heading, depending on the time of death. According to this unifying hypothesis the pathogenesis of isolated myocarditis is seen as a succession of acute episodes of cardiac muscle injury associated with protracted interstitial reaction. Differences in the severity of the initial injury, variable secondary changes and death fortuitously at any stage of the disease would operate to produce the diverse histological appearances which have been described in different cases.

Summary

Two fatal cases of acute isolated myocarditis occurring in newborn infants are described.

The lesions in the myocardium were focal in distribution and showed a peculiar degenerative

change limited to the sarcoplasm of the affected muscle fibres.

The relationship of this parenchymatous lesion to the commoner interstitial type is discussed.

There was no response to treatment with various antibiotic agents.

Thanks are due to Dr. Muriel Frazer who has allowed me to make use of the material from Case 2.

References

Biggart, J. H. (1950). *Ulster med. J.*, **19**, 59.
Boikan, W. S. (1931). *Virchows Arch.*, **282**, 46.
Fiedler, A. (1899). 'Festschrift zur Feier des 50 jahrigen Bestehens des Stadtkrankenhauses zu Dresden-Friedrichstadt.' Dresden.
Gouley, B. A., McMillan, T. M. and Bellet, S. (1937). *Amer. J. med. Sci.*, **194**, 185.
Lemke, R. (1924). *Virchows Arch.*, **248**, 345.
Lind, J. and Hultquist, G. T. (1949). *Amer. Heart J.*, **38**, 123.
Millar, W. G. (1933). *J. Path. Bact.*, **37**, 127.
Saphir, O., Wile, S. A. and Reingold, I. M. (1944). *Amer. J. Dis. Child.*, **67**, 294.
Sellentin, L. (1904). *Z. klin. Med.*, **54**, 298.
Singer, L. (1932). *Z. Kinderheilk.*, **53**, 660.

THIRTY-EIGHT CASES OF HAEMOLYTIC DISEASE OF THE NEWBORN

BY

Z. SHAMIR and J. GUREVITCH

From the Departments of Paediatrics and Clinical Microbiology of the Hebrew University-Hadassah Medical School, Jerusalem

(RECEIVED FOR PUBLICATION MARCH 9, 1953)

The following is a report of the clinical and laboratory findings and the therapeutic results in 38 cases of haemolytic disease of the newborn which were observed at the Rothschild-Hadassah-University Hospital during the years 1946-52.

Material and Methods

Thirty of the 38 cases were the result of Rh sensitization, and eight were due to incompatibility in the ABO system.

Prenatal Investigations. Pregnant women attending the health centres, which combine the functions of prenatal and infant welfare clinics, were examined routinely for Rh blood groups. The Rh-negative women were tested for Rh antibodies. Cases with Rh antibodies were invited to attend for monthly control titrations during the second trimester, and twice a week during the last trimester of pregnancy.

In a similar way serial antibody determinations for anti-A or anti-B were carried out during pregnancy in all cases with a previous history of iso-immunization and erythroblastotic infants due to ABO incompatibility. The blood group and Rh type of the father's red cells were also determined in all cases of suspected iso-immunization.

Rh antibodies in maternal sera were examined in saline and plasma. In the second part of this study the Coombs indirect method was also used. In several instances trypsinized cells were examined (Morton and Pickles, 1947).

Neonatal Investigations. Cord blood was studied in those cases in which the past history of the mother or the laboratory studies during pregnancy suggested the possibility of haemolytic disease of the newborn infant. In all cases not preceded by prenatal examinations the infant's venous blood was tested immediately following the first appearance of signs of haemolytic disease. The examinations included blood group and Rh type determinations, the direct Coombs test and a blood count.

Method of Treatment. In previous years cases of erythroblastosis foetalis have been treated by simple transfusions—single or multiple—of Rh-negative blood, or of group O-blood in instances due to ABO incompatibility.

Since 1950 exchange transfusion has been carried out in all cases in which the previous history and the clinical and laboratory findings suggested the possibility of a severe form of haemolytic disease in the newborn infant. For exchange transfusion, generally, the technique as recommended by Diamond (1947) and Mollison, Mourant and Race (1948) was used. A plastic catheter was introduced into the umbilical vein and the blood was exchanged by the 20 ml.-out 20 ml.-in method. If more than 12 hours had elapsed after birth the vena cava was entered through the saphena magna vein in the groin and the femoral vein according to the technique described by Arnold and Alford (1948).

In two instances, owing to the technical difficulties, the umbilical route had to be abandoned for the withdrawal of blood. The remainder of the blood was withdrawn from the sagittal sinus through the anterior fontanelle. In general, from 400 to 500 ml. of donor blood was used for replacement, leaving a surplus of about 50 ml. of transfused blood above the amount of withdrawn blood.

I. Rh Incompatibilities

Incidence. There were 29 cases of haemolytic disease of the newborn among 10,800 deliveries, an incidence of 1 in 372, during the years 1946-52, excluding 1948. For the year 1948 records were incomplete as a result of war conditions. In this year one case of haemolytic disease was found and is not included in the incidence calculation but is included in this series.

This relatively low incidence rate may have been due to the fact that primiparas were particularly selected for delivery at our maternity ward and

represented, therefore, a disproportionate percentage of the total number of deliveries. Previously Gurevitch, Brzezinski and Polishuk (1947) reported an incidence of 1 in 2,100 deliveries among Jerusalem Jews. The present apparently increased incidence of 1 in 372 may be attributed to expanded facilities for laboratory diagnosis.

Sex. There were 16 male and 14 female infants. Eleven (69%) of the male infants and 11 (79%) of the female infants recovered. Although this number of cases is too small to permit conclusions, no significant difference of mortality and recovery rates in both sexes was observed.

Past History of the Mother. Twenty-nine of 30 erythroblastotic infants were born to multiparas, and only one case—a stillborn infant—was the result of the first pregnancy of an Rh-negative woman. In this case no transfusion or blood injection was known to have been given to the woman previously. A titre of 1 in 512 for saline anti-Rh antibodies was found in the mother's serum shortly after delivery. Two years later the same woman gave birth to an infant severely affected by haemolytic disease.

In one case a blood transfusion appeared to have acted as the first sensitization against the Rh factor, and was followed by stillbirth after a first pregnancy and an erythroblastotic infant after the second pregnancy.

One case appeared to be an instance of late sensitization, since the erythroblastotic child, born of the fourth pregnancy, was preceded by three normal unaffected siblings. In this instance complete recovery occurred without any treatment. Allen, Diamond and Vaughan (1950) have suggested that such cases of 'late sensitization' show a milder course of the haemolytic disease.

Jaundice. Except for three mild cases, almost all liveborn infants in this series exhibited jaundice during the first 24 hours after birth. The exact time of appearance of jaundice was as follows:

At birth	6 cases
4-12 hours after birth	9 „
12-24 hours after birth	6 „
Second day	2 „
No jaundice	3 „

It is of interest that six infants had jaundice at birth. In the series reported by Diamond, Vaughan and Allen (1950) there was no case of jaundice at birth.

The three infants without jaundice were mild cases with signs of anaemia only, so-called 'congenital anaemia'. Two of them recovered spontaneously, the third after a simple transfusion.

Spleen and Liver Enlargement. The spleen was found enlarged (over 2 cm. below the costal margin) in 18 cases, normal in three. The liver was enlarged in 12 cases, normal in nine. In five cases exact data on the size of spleen and liver were not available. In the remaining four cases the infants were stillborn.

Direct Coombs Test. Of the 19 cases examined by the antiglobulin test, 14 showed positive results. The first three cases yielded negative results which may have been due to inadequate technique at the beginning in using the Coombs test. Two other cases, siblings, presented the problem of double incompatibility.

Anaemia. Blood counts throughout the whole series ranged from 1,300,000 to 4,500,000 red cells per c.mm., and from 6·5 g. to 15 g. of haemoglobin per 100 ml. of blood, with the majority of cases on the lower side of the range. An abnormally elevated number of nucleated red cells was found in all but three cases.

No definite correlation between the degree of anaemia or the number of nucleated red cells and the severity and prognosis was found.

Serological Findings in Maternal Sera. An analysis of the serological findings revealed no clear correlation between the titre of Rh antibodies in the maternal sera and the severity of haemolytic disease in the newborn infant. Thus, two cases suffered from mild haemolytic disease in presence of a high antibody titre, while another case resulted in the death of the affected infant in the presence of a relatively low antibody titre in the mother's serum. It is noteworthy, however, that all cases of stillbirth in this series were accompanied by especially high antibody titres in the respective mother's serum.

A special problem is represented by the cases of double incompatibility in the Rh- and ABO-system at the same time. These cases were characterized by the absence of Rh antibodies and by low anti-A or anti-B titres in the maternal serum. Despite these findings, the typical picture of severe haemolytic disease existed in the infants, and in one case resulted in kernikterus and death of the infant. The inhibition of antibody formation may possibly be due to 'competition of antigens' as suggested by Wiener (1945). It is of interest that the Coombs test was also negative in two of these cases.

II. ABO Incompatibilities

A review of the literature on this subject showed that up to now no clear-cut opinion on the validity of 'ABO erythroblastosis' has been reached. Thus Pickles (1949) believed that 'only very stringent tests for incomplete antibodies anti-A and anti-B, and the exclusion of other haemagglutinins in each case can give unequivocal proof of ABO erythroblastosis'. Zuelzer and Mudgett (1950) were of the opinion that a rise in anti-A or anti-B titre and the detection of

TABLE
FINDINGS IN EIGHT CASES OF ERYTHROBLASTOSIS

Year	Case	Sex	Pregnancy	Previous History and Sensitization of Mother	Clinical Findings			Blood Group M = mother I = infant F = father
					Jaundice	Enlarged Spleen	Enlarged Liver	
1947	1	F.	4	2 normal children 1 stillbirth	2nd day	–	–	M: OCDe/cde I: ACDe/cde F: ACDe/cde
1950	2	F.	3	2 normal children		Stillbirth		M: OCDe/cde I: ? F: ACDe/cde
	3	M.	3	1 abortion 1 premature infant, died	2nd day	+	–	M: OCDe/CDe I: ACDe/CDe F: ACDe/CDe
1951	4	M.	4	See case 3 above; induction of labour 39th week	At birth	–	–	M: OcDE/cde I: ACDe/cde F: ACDe/CDe
	5	F.	6	1 child died immediately after birth, 2 children died at later age 2 normal children	5 hours	+	+	M: OCDe/cDE I: BCDe/cde F: BCDe/cde
	6	F.	1		8 hours	–	–	M: OcDE/cde I: Acde/cde F: ?
	7	M.	1		10 hours	–	–	M: OCDe/cde I: ACDe/CDe F: ?
1952	8	M.	1		At birth	+	–	M: OCDe/cde I: BcDE/cde F: BcDE/cde

incomplete antibodies were not sufficient criteria to establish the validity of ABO erythroblastosis, as they could be found commonly in normal heterospecific pregnancies. On the other hand, Wiener, Wexler and Hurst (1949) were impressed by the growing number of well documented reports of typical and sometimes fatal cases as evidence for AB sensitization in the aetiology of haemolytic disease of the newborn.

Despite the difference of opinion on this subject, and although we feel that doubts are justified as long as no more accurate proof of the validity of ABO erythroblastosis can be established, our series adds another eight cases of typical haemolytic disease of the newborn in which no Rh incompatibility existed and in which AB sensitization appeared to be the probable aetiology. Other factors, however, could not be completely excluded, as we were not equipped with facilities for investigations of other antigenic systems.

Findings in the ABO group of cases are summarized in Table 1.

With regard to the past history of mothers, the composition of this group was different from the Rh group. Four of the eight cases of haemolytic disease occurred as a result of first pregnancies and without a history of previous blood transfusion. These cases, therefore, exemplify the peculiarity of 'ABO erythroblastosis' which occurs occasionally in first pregnancies (Pickles, 1949).

Jaundice appeared immediately at birth in two of the cases, and up to the second day in the remainder of cases. The Coombs test was negative in all of our cases. The inadequacy of the Coombs test for the detection of univalent anti-A or anti-B has been repeatedly stressed by various authors, and remains as yet unexplained (Coombs, Mourant and Race, 1946; Wiener *et al.*, 1949). Progressive anaemia and the presence of many nucleated red cells in the peripheral blood was a common feature of our cases.

As seen from Table 1, incomplete anti-A or anti-B titres in maternal sera ranged from 2,000 to 128,000 units in plasma. While Smith (1945), Tovey (1945) and Zuelzer and Mudgett (1950) have pointed to the fact that high titres may occur in normal heterospecific pregnancies without any pathological effect on the foetus, Wiener *et al.* (1949) have shown a much higher range of titre in cases of affected infants as compared with a series of unaffected infants from heterospecific pregnancies.

Although it seems established that high univalent anti-A or anti-B titres *per se* are not necessarily

FOETALIS DUE TO ABO INCOMPATIBILITY

Laboratory Findings: Infant — Direct Coombs	R.B.C. (in millions)	Hb. (g.)	Nucleated R.B.C. (per cent. of total nucleated cells)	Maternal Anti-Bodies (in units): Saline	Plasma	Treatment	Results	Remarks
?	2·8	8	50	anti-A 16,000	32,000	Simple transfusion at 4 weeks	Died	Late admission to hospital
?				anti-A 2,000	16,000		Stillbirth	
—	2·6	15	0	anti-A 1,000	4,000	Simple transfusion on fourth day	Died (kernikterus)	Late admission to hospital
—	5·5	15	30	anti-A 2,000 anti-C 0	16,000 0	Exchange transfusion	Recovered	Induction of labour 39th week
—	4·2	12	37	anti-B 128	2,000	Simple transfusion	Recovered	Premature birth (2,300 g.)
—	2·6	9	40	anti-A 256	128,000	Simple transfusion	Recovered	
—	3·8	12·5	0	anti-A 512 trypsin cells 2,000	512	Simple transfusion	Recovered	
—	2·7	11·5	11	anti-B 512 anti-E 0	1,000 0	Simple transfusion	Recovered	

correlated with a diseased infant, only such high titres may warrant the designation of cases as haemolytic disease possibly due to ABO incompatibility. In view of this criterion, cases with lower titres were not included in this series. Of the fatal cases in this group, one was a stillbirth, and two died after inadequate treatment (Nos. 1, 3). The mother of cases Nos. 3 and 4 was of special interest. During her pregnancy in 1950 (Case 3) her plasma titre of anti-A antibodies was 4,000. The infant of this pregnancy died of haemolytic disease. In the following year, during another pregnancy (Case 4) the plasma titre of anti-A antibodies rose to 16,000. Labour was induced in the thirty-ninth week of gestation. Despite the increased titre of anti-A antibodies and the increased severity of the haemolytic disease in Case 4, the infant recovered following exchange transfusion.

III. Treatment

The indication for treatment was based on clinical and haematological grounds and was independent of whether the underlying cause was found to be Rh or ABO incompatibility.

Of the 33 liveborn infants, 16 were treated by simple transfusions, 13 by exchange transfusion and four mild cases recovered spontaneously. Of the group of 16 infants who received simple blood transfusions, five died. The 13 infants treated by exchange transfusion all recovered despite the fact that the more severe cases were selected for this treatment (Table 2).

TABLE 2

RESULTS OF TREATMENT IN 33 CASES OF HAEMOLYTIC DISEASE OF THE NEWBORN

	Simple Transfusion	Exchange Transfusion	No Treatment
Recovered ..	11	13	4
Died	5	–	–
Total	16	13	4

The difficulty of evaluating and comparing various methods of treatment of haemolytic disease of the newborn has been repeatedly pointed out (Vaughan, Allen and Diamond, 1950). It is primarily due to the fact that the early estimation of the severity of a case of haemolytic disease is usually most difficult. Nevertheless from our figures, though small, the conclusion may be drawn that exchange transfusion proved to have a definite advantage in the treatment of haemolytic disease of the newborn, and represented therefore the treatment of choice for all severe

cases of this disease. It has to be borne in mind, however, that in three cases out of the five deaths in the group of simple transfusions treatment was started relatively late, and that early simple transfusion perhaps might have changed the final outcome of these cases.

The value of exchange transfusion for severe cases and the adequacy of early, simple transfusion for milder cases has been convincingly worked out in the recent controlled trials of treatment by Mollison and Walker (1952).

Induction of labour in our series was performed in two cases only, in both of them because of the history of previous fatal haemolytic disease in several siblings, and rise in antibody titre in the mother's serum during pregnancy. In both instances labour was induced in the thirty-ninth week of gestation, and resulted in a living erythroblastotic infant who recovered after exchange transfusion.

Summary

Clinical, haematological and serological findings, and the therapeutic results in a series of 38 cases of haemolytic disease of the newborn are reported. Of these, 30 were due to Rh incompatibility, and eight to ABO incompatibility.

The problem of ABO incompatibility in the aetiology of haemolytic disease of the newborn is discussed.

We wish to thank Dr. E. Rabinovich, Head of the Newborn Department of the Rothschild-Hadassah-University Hospital, for his kind permission to use the clinical data published in this paper.

References

Allen, F. H. Jr., Diamond, L. K. and Vaughan, V. C. III (1950). *Pediatrics*, **6**, 441.
Arnold, D. P. and Alford, K. M. (1948). *J. Pediat.*, **32**, 113.
Coombs, R. R. A., Mourant, A. E. and Race, R. R. (1946). *Lancet*, **1**, 264.
Diamond, L. K. (1947). *Proc. roy. Soc. Med.*, **40**, 546.
——, Vaughan, V. C. III and Allen, F. H., Jr. (1950). *Pediatrics*, **6**, 630.
Gurevitch, J., Brzezinski, A. and Polishuk, Z. (1947). *Lancet*, **2**, 943.
Mollison, P. L., Mourant, A. E. and Race, R. R. (1948). *Med. Res. Coun. Lond.* Memorandum No. 19. H.M.S.O., London.
—— and Walker, W. (1952). *Lancet*, **1**, 429.
Morton, J. A. and Pickles, M. M. (1947). *Nature, Lond.*, **159**, 779.
Pickles, M. M. (1949). *Haemolytic Disease of the Newborn*. Oxford.
Smith, G. H. (1945). *J. Path. Bact.*, **57**, 113.
Tovey, G. H. (1945). *Ibid.*, **57**, 295.
Vaughan, V. C. III, Allen, F. H., Jr. and Diamond, L. K. (1950). *Pediatrics*, **6**, 173.
Wiener, A. S. (1945). *Proc. Soc. exp. Biol., N.Y.*, **58**, 133.
——, Wexler, I. B. and Hurst, J. G. (1949). *Blood*, **4**, 1014.
Zuelzer, W. W. and Mudgett, R. T. (1950). *Pediatrics*, **6**, 452.

A CASE OF CONGENITAL DIABETES

BY

MARY E. S. WYLIE

From the Department of Child Health, University of Glasgow, and the Royal Hospital for Sick Children, Glasgow

(RECEIVED FOR PUBLICATION MARCH 29, 1953)

Diabetes mellitis is relatively rare in infancy although it was diagnosed in an infant in 1789. Schwartzmann, Crusius and Beirne (1947) reviewed 57 cases with the onset of symptoms in the first year of life. In 1952 Brodribb, McMurray and Scott reported two further cases.

During the first four weeks of life diabetes has been diagnosed on seven occasions, although the diagnostic criteria are open to doubt in some of the cases. The first was described by Kitselle (1852) in his own son who shortly after birth showed polyuria, polydipsia, emaciation and glycosuria, and who died after a few months. The second, recorded in 1910 by Cuno, was in a 15-day-old baby with glycosuria and hyperglycaemia. Necropsy showed atrophy of the pancreas. Ramsey, in 1926, reported the case of a 4-week-old premature baby presenting with excessive appetite and thirst, glycosuria and hyperglycaemia who appeared to recover completely in six weeks. Four years later this child had a normal glucose tolerance curve. Lawrence and McCance (1931) reported the case of an 18-day-old baby with gangrene of the leg who had glycosuria and a blood sugar level of 600 mg. per 100 ml. At 6 weeks of age this child appeared to recover spontaneously. Two cases have been recorded in Negro infants. Lewis and Eisenberg (1935) reported the case of a baby who had otitis media and bullous impetigo and was found to have glycosuria and a blood sugar level which varied between 280 and 520 mg. per 100 ml. Limper and Miller (1935) reviewed the case of a child with gangrene of the leg, glycosuria and a blood sugar level of 952 mg. per 100 ml. Neither of these infants survived long, in spite of insulin therapy. Atrophy of the pancreas was present in both cases. From this hospital in 1938 Devine described a 25-day-old premature baby who failed to thrive and on admission was found to have glycosuria and a blood sugar level of 542 mg. per 100 ml. The patient died before treatment could be instituted.

Case Report

A girl, aged 17 days, was admitted to hospital from a maternity home on May 15, 1952, because of failure to thrive in spite of feeds adequate in calories, which were taken eagerly. The provisional diagnosis was fibrocystic disease of the pancreas.

She was the first born child of young healthy parents from whom no history of familial diabetes or consanguinity could be obtained. The pregnancy was uncomplicated and the delivery normal but, though born at full term, the infant's birth weight was only 2·4 kg, (5 lb. 5 oz.). The baby's condition immediately after birth gave no anxiety. At first she was reluctant to fix on the breast so she was fed with expressed breast milk. After a few days she sucked well but, despite a voracious appetite and the absence of any vomiting or diarrhoea, she steadily lost weight. On the assumption that she had a subclinical infection she was given a course of aureomycin without any improvement.

On admission to hospital the baby weighed 1·765 kg. (3 lb. 14 oz.) and presented a remarkable appearance of senility (Fig. 1). There was gross emaciation and dehydration, the face was wrinkled and wizened, the fontanelle was sunken and the skull sutures were overriding. There was no evidence of infection. The liver edge was palpable one fingerbreadth below the costal margin, and the lower poles of both kidneys and the spleen were just palpable. There were no clinical signs of ketosis and, despite her very poor general condition, the baby was surprisingly alert, crying quite vigorously and eager to suck. Retinoscopy and electrocardiography did not reveal any abnormality.

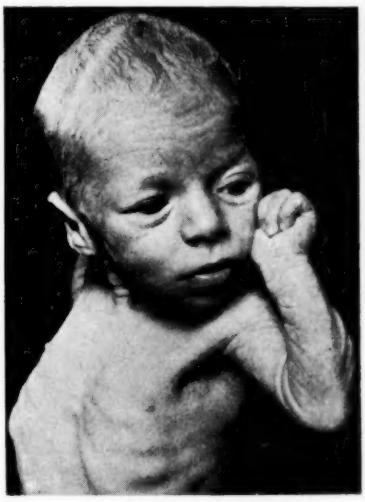


FIG. 1.—Appearance on admission to hospital at the age of 17 days.

The urine contained a trace of albumin, completely reduced Benedict's reagent, but did not contain ketones. The blood sugar level was 666 mg. per 100 ml. The blood

galactose level was normal and only glucosazone crystals were recovered from the urine.

Ten units of soluble insulin were given intramuscularly and two hours later the blood sugar level was 708 mg. per 100 ml. After two further doses, each of 10 units, the blood sugar level had fallen to 102 mg. per 100 ml. 16 hours after admission. After the start of insulin therapy the baby stopped sucking and feeds (half-cream National Dried Milk, 60 ml., plus sugar, 5 g., four-hourly) had to be given by tube. An intravenous infusion of quarter strength physiological saline with 5% glucose was given at the rate of 10 ml. per hour (2 oz. per pound of body weight per 24 hours). Intramuscular soluble insulin was continued, 5 or 10 units before feeds, according to the sugar levels in the blood and urine. After 72 hours of treatment the infant was improved and again sucked vigorously so intravenous fluids were discontinued.

Stabilization proved even more difficult than anticipated and it was found necessary to give insulin four-hourly before feeds. On a feeding regime of half-cream National Dried Milk, 105 ml., plus sugar, 5 g., four-hourly, and 3 units of soluble insulin intramuscularly before feeds, hourly blood sugar levels over a 24-hour period fluctuated between 266 mg. and 16 mg. per 100 ml. Ketonuria was consistently absent even when the urine was loaded with sugar and the blood sugar was 600 mg. per 100 ml. In the first few weeks typical hypoglycaemic attacks occurred frequently. During several of these episodes blood sugar levels of less than 10 mg. per 100 ml. were recorded. On each occasion the attack was terminated when glucose, 10-20 g. was given by stomach tube, save in one attack when 3 minims of subcutaneous adrenalin were required to restore consciousness.

When 5 weeks old she developed a mild anaemia (Hb, 9·1 g.), doubtless aggravated by frequent blood sugar estimations, and a transfusion of 75 ml. of blood was given which raised the haemoglobin to 15·4 g.

Despite these initial difficulties the baby gained weight rapidly and as her weight increased so the wrinkles were erased from her face. At the age of 8 weeks she was apparently well controlled on half-cream National Dried Milk, 120 ml., plus sugar, 10 g., offered four-hourly (total calories 600), and 5 units of insulin before each feed. Her weight was then 3·32 kg. (7 lb. 5 oz.). She seemed mentally normal and interested. At this point she was discharged from hospital on June 24, 1952, to abolish the risk of possible cross-infection. Her mother had mastered with admirable fortitude the technique of insulin injection. During the next two weeks she gained 0·61 kg. (1 lb. 5 oz) but the strain on her mother was so severe that she was readmitted on July 4, 1952, in order that the 2 a.m. feed and injection could be omitted. She was then gradually changed from half to full-cream National Dried Milk and the insulin dosage was re-adjusted to 3 units of soluble before each four-hourly feed (five times daily). Her weight was then 4·55 kg. (10 lb.) and she was again returned to her mother's care. During the next 14 weeks she was supervised as an out-patient, the insulin requirements remaining constant, while the feeds were increased gradually and solid foods introduced. At 20 weeks old, on December 7, 1952, the baby was readmitted for reassessment, and over four days' observation was found to have irregular glycosuria and blood sugar levels which fluctuated from 420 mg. to 40 mg. per 100 ml. The soluble insulin dosage was maintained at 3 units, five times daily. On January 7, 1953, a glucose tolerance curve was carried out and gave the following results.

	Sugar Levels (mg./100 ml.)
Before glucose	80·6
½ hour after glucose	181·8
1 hour after glucose	196·0
1½ hours after glucose	222·2
2 hours after glucose	235·2

Now 8 months old (Fig. 2) the baby weighs 9·55 kg. (21 lb.) and is on a normal mixed diet. The insulin dosage is unchanged. She is a happy and contented child reacting normally to her surroundings.

FIG. 2.—Appearance at the age of 8 months.

Comments

It seems probable that this child is an example of true pancreatic diabetes because of her dramatic and sustained improvement on insulin. Though born at full term, her birth weight was only 2·4 kg. (5 lb. 5 oz.). This might suggest that the disease was present *in utero* and that the mother's insulin proved insufficient for herself and the foetus.

In some of the cases reviewed the diagnosis of diabetes mellitus would appear to be in some doubt. For example, in the cases described by Ramsey (1926) and Lawrence and McCance (1931) there was a complete and spontaneous remission. In other cases, for example those described by Lewis and Eisenberg (1935) and Limper and Miller (1935), the glycosuria and high blood sugar levels were associated with an infection. In the present case there was no obvious clinical sign of infection. It is a striking fact that in all the reported cases, even those with the most marked glycosuria, there was no acetone in the urine. It is interesting to note that the present patient was alert and sucking when the blood sugar level was 706 mg. per 100 ml.

In all the cases of diabetes during the neonatal period so far reported, excluding the two which recovered spontaneously, the mortality was 100% before the age of 6 months. The immediate prognosis of the patient here reported seems now to be good. The ultimate prognosis cannot be assessed.

Summary

Seven cases of diabetes mellitus with the onset in the neonatal period are reviewed.

A patient diagnosed at 17 days, treated with insulin and thriving at 8 months, is described.

Thanks are due to Dr. J. H. Hutchison for permission to publish this case and for his advice and criticism.

References

Brodribb, H. S., McMurray, J. and Scott, L. G. (1952). *Brit. med. J.*, **1**, 1060.
Cuno, F. (1910). *Jb. Kinderheilk.*, **71**, 623.
Device, J. (1938). *Archives of Disease in Childhood*, **13**, 189.
Kitselle, J. F. (1852). *Jb. Kinderheilk*, **18**, 313.
Lawrence, R. D. and McCance, R. A. (1931). *Archives of Disease in Childhood*, **6**, 343.
Lewis, E. and Eisenberg, H. (1935). *Amer. J. Dis. Child.*, **49**, 408.
Limper, M. A., and Miller, A. J. (1935). *Ibid.*, **50**, 1216.
Ramsey, W. R. (1926). *Trans. Amer. pediat. Soc.*, **38**, 100.
Schwartzman, J., Crusius, M. E. and Beirne, D. P. (1947). *Amer. J. Dis. Child.*, **74**, 587.

RENAL THROMBOSIS COMPLICATING PINK DISEASE: CURE BY NEPHRECTOMY

BY

W. G. Q. MILLS and T. K. OWEN

From the Royal Victoria Hospital, Bournemouth

(RECEIVED FOR PUBLICATION APRIL 13, 1953)

Renal thrombosis is an uncommon complication of pyelitis in infancy. A record is therefore presented of the following case, in which a cure was obtained by surgical excision of an infarcted kidney, occurring in the course of pyelitis complicating pink disease.

Case Report

S.R., age 18 months, was admitted in April, 1952, giving a typical history of pink disease of six weeks' duration. Her further progress was variable and the course of the illness was complicated by intercurrent infections. In May she had gastro-enteritis, and was treated with chloromycetin. In July she had a severe upper respiratory tract infection, severe ulceration of toes and fingers, and right lower lobe pneumonia. This was treated by aureomycin. In August she had severe ulceration of the mouth and tongue, with a large slough on the anterior third of the tongue. On August 16 she developed a severe attack of pyelitis, the urine containing *Bact. coli* and *Proteus*. Aureomycin was given again, but the child's condition remained very poor. She became extremely emaciated and had large ulcers in the mouth and on the extremities. On September 18 she suddenly collapsed, and although she improved with stimulants, she developed aspiration pneumonia, again treated by aureomycin. On September 22 her condition was very poor, and she had gross haematuria. The blood urea level was 111 mg. %, and *Bact. coli* was present in the urine. On September 23 a hard irregular mass was first felt in the left renal angle. A tentative diagnosis of renal embryoma (Wilms' tumour) was made. On September 29 the left kidney was removed. The child slowly improved after the operation, although *Proteus* persisted in the urine for some time. When seen in November she was perfectly well and had gained 2 lb. in weight.

PATHOLOGICAL REPORT. The kidney (Figs. 1 and 2) was enlarged, dark red and engorged (weight, 136 g., expected normal weight, 43 g.; $8{\cdot}5 \times 5{\cdot}5 \times 5{\cdot}0$ cm. in maximum diameters).

The capsule was slightly thickened and its inner surface was lined by a layer of partially organized inflammatory exudate. The renal parenchyma cut easily and the central portion was composed of congested tissue in which there were many pale, greyish-yellow areas of infarction surrounded by haemorrhagic zones. Towards the hilum

FIG. 1.—Outer surface of Kidney.

many thrombosed veins were visible, but no arterial abnormality could be seen. Microscopic examination showed areas of recent haemorrhage, areas of complete infarction, and small zones of surviving parenchyma,

FIG. 2.—Cut surface of Kidney.

which were infiltrated diffusely with inflammatory cells and in which there was considerable interstitial oedema. Collections of organisms were present in some of the infarcted tissue and in several small arterioles. Most veins were abnormal and contained ante-mortem thrombus, some of which was recent, but some showed early organization. The arteries and arterioles in general were very much less affected than the veins, and quite a high proportion of them were entirely normal. The pelvic tissues were acutely inflamed, and the small veins deep to the pelvic epithelium were thrombosed.

It was concluded that the condition was venous thrombosis supervening on acute (probably haematogenous) pyelonephritis.

Discussion

Campbell and Matthews (1942) reviewed the literature concerning renal thrombosis in infancy, and reported two cases successfully cured by nephrectomy. In their first patient, aged 13 days, a tentative diagnosis of Wilms' tumour was made, as in the case here reported, but in their second, aged 33 days, a pre-operative diagnosis of renal thrombosis was confirmed. They pointed out that the condition was not as rare as the sporadic cases reported in the literature would suggest, and that many cases pass unrecognized under the inadequate diagnosis of acute pyelitis or profound sepsis. Without operation, the prognosis is extremely grave, but it is possible that survival may occasionally occur, resulting in the unilateral scarred, atrophied kidney that is sometimes found in adult life.

Sandblom (1948) reported the successful removal of an infarcted kidney from a 5-day-old infant. He attributed the thrombosis of the renal veins to birth trauma by a difficult forceps delivery. He points out that renal infarction in children appears in two forms with different aetiology, (1) secondary to birth trauma, and, (2) the more common form, secondary to infection with dehydration. Kobernick, Moore and Wiglesworth (1951) reported four further cases, all diagnosed at necropsy, aged 3 weeks, 14 months, 2 months and 1 month. The present case is the fourth recorded successfully treated by operation, and with the exception of the second case of Kobernick *et al.*, we have not found any record of the condition occurring in the second year of life.

In our case the child had been suffering from *Bact. coli* and *Proteus* pyelitis for a little over four weeks, when she suddenly collapsed. It is probable that it was at this stage that the infection spread to a branch of the renal vein, initiating the thrombosis. Four days later severe haematuria was noted, and the next day a hard mass was felt in the loin.

Attention is drawn to the fact that if a hard mass suddenly becomes apparent in the loin of an infant suffering from pyelitis, it may be due to renal vein thrombosis, and the condition is amenable to surgery.

We wish to express our thanks to Dr. D. W. Beynon, under whose care the child was admitted, for the clinical notes, and to Dr. R. C. B. Pugh of the Hospital for Sick Children, Great Ormond Street, London, for help with the pathological report and the photographs.

REFERENCES

Campbell, M. F. and Matthews, W. F. (1942). *J. Pediat.*, **20**, 604.
Kobernick, S. D., Moore, J. R. and Wiglesworth, F. W. (1951). *Amer. J. Path.*, **27**, 435.
Sandblom, P. (1948). *Acta. paediat., Uppsala*, **35**, 160.

HAEMORRHAGIC INFARCTION OF THE KIDNEY TREATED BY NEPHRECTOMY

BY

C. DENLEY CLARK and J. D. PICKUP

From the Clayton Hospital, Wakefield

(RECEIVED FOR PUBLICATION MARCH 13, 1953)

A review of the literature indicates that successful nephrectomy for haemorrhagic infarction of the kidney has been reported in only five instances. In America Campbell and Matthews (1942) described two cases and Milburn (1952) one case, in Sweden Sandblom (1948) described one, while in this country the only case record is by Parry (1951). The occurrence of a further case is thought worthy of record.

Case Report

S.P. was a full term female infant born on January 23, 1952, weighing 7 lb. Two days later she developed a pustule behind the ear. She was treated with chloramphenicol but the lesion progressed to form an abscess which was incised. On February 2 the baby became very fretful and developed a temperature of 100° F.

On examination slight evidence of dehydration was noted and there was marked harlequin mottling of the skin. The kidney was enlarged and easily palpable in the left loin.

The urine contained much albumin and a few red cells on microscopic examination. The urine was sterile on culture.

Blood examination gave haemoglobin, 98% (Haldane); red blood cells, 4,600,000 per c.mm.; white blood cells, 22,000 per c.mm. (polymorphs 50%, lymphocytes 47%, monocytes 3%). On February 5 the blood urea concentration was 40 mg.%.

Diodranil was given intramuscularly, but the pyelograms were unsatisfactory.

In view of these findings, it was felt that the diagnosis lay between a perinephric abscess, congenital hydronephrosis or a renal infarct.

The operation was performed on February 5, 1952, under general anaesthesia. A left lumbar incision was used. The left kidney was enlarged and completely infarcted, presenting as a friable mass of blood clot, in which it was almost impossible to distinguish any renal tissue. The left renal vein was thrombosed, but there was no evidence of thrombosis in the vena cava. Left nephrectomy was performed. Post-operatively 100 ml. of 1 in 5 normal saline was given subcutaneously.

The post-operative course was rather stormy for the next three days. Slight sepsis in the wound responded to treatment with streptomycin. The baby, fed on expressed breast milk, was at first slow in taking the feeds, but gradually feeding at the breast was re-established. On February 6 the blood urea level was 54 mg.% and by February 11 it had fallen to 29 mg.%. The urine contained only a trace of albumin and no red blood cells on February 16. By March 11 the blood urea level had risen to 80 mg.% and on July 10 to 90 mg.%, but the urine was clear of albumin and blood.

The child is now active and feeding well and at 1 year of age weighs 18 lb. 15 oz. The blood urea level had fallen to 30 mg.% on January 22, 1953.

Pathological Report. Dr. W. L. Rose reported as follows:

'The kidney was submitted for examination in a fragmented condition. The parenchyma was firm and red, having the appearance of an infarction. Histological examination of the kidney shows gross parenchymatous haemorrhage, which is causing disruption of the renal tissue. Towards the cortex of the kidney the haemorrhage is less and the glomerular and the tubular architecture is "living" and reasonably well defined. Search throughout the sections reveals early organizing venous thrombi. I am of the opinion that this is an infarction of the kidney due to extensive venous thrombosis of the renal veins.'

Discussion

In retrospect the diagnosis of renal infarction could have been made with more certainty in view of the previous history of sepsis associated with the clinical findings, and the presence of albumin and red blood cells in the urine. It should be emphasized that the urine was never macroscopically blood-stained, nor was it infected, although both these features are regarded by Parry (1951) as being points helpful in making the diagnosis.

A rise in the blood urea level after operation is in keeping with the experience of Milburn (1952), who believes that this is due to the occurrence of lower nephron nephritis in the remaining kidney. Although there was a persistent azotaemia in our case for six months, there was no accompanying albu-

minuria, the absence of which would be unlikely in a lower nephron nephritis.

Summary

A case of unilateral renal thrombosis occurring in the neonatal period is described.

We are grateful to Dr. W. L. Rose for his histological and biochemical reports, and to Mr. J. M. McKiddie for access to his case records.

References

Campbell, M. F. and Matthews, W. F. (1942). *J. Pediat.*, **20**, 604.
Milburn, C. L. (1952). *Ibid.*, **41**, 133.
Parry, E. W. (1951). *Archives of Disease in Childhood*, **26**, 358.
Sandblom, P. (1948). *Acta paediat., Uppsala*, **35**, 160.

PAPULAR URTICARIA

BY

ARTHUR ROOK and W. FRAIN-BELL

From the Department of Dermatology, United Cardiff Hospitals

(RECEIVED FOR PUBLICATION APRIL 24, 1953)

Papular urticaria is one of the commonest and most troublesome skin diseases of early childhood. The controversy as to whether the eruption is of parasitic origin or whether it is related to digestive disturbances, allergic or otherwise, is now approaching its centenary and is still vigorously debated. The inconsistent response to our own therapeutic efforts prompted us to study a series of cases in some detail and to review the literature which, for so common a condition, is surprisingly scanty.

Clinical Description

Thomas Bateman in 1813 wrote:

> 'There is scarcely any limit to the varieties of these papular affections, but I have observed one form which is so uniform in its character as to be entitled to notice here. It might be called lichen urticatus; its first appearance is in irregular inflamed wheals, so closely resembling the spots excited by the bites of bugs or gnats as almost to deceive the observer. The inflammation, however, subsides in a day or two leaving small, elevated, itching papules. While the first wheals are thus terminating new ones continue to appear in succession until the whole body and limbs are spotted with papules which become here and there confluent in small patches. The eruption is peculiar to children: it commences in some cases soon after birth and sometimes later and continues with great obstinacy for many months. Both the wheals and the papules are accompanied by intense itching, which is exceedingly severe in the night, occasioning an almost total interruption of sleep and a considerable loss of flesh.'

Although later observers have added to our knowledge of the natural history of the condition, this clinical description is still among the best available.

Willan and his pupil Bateman made an effort to place the morphological description of skin lesions on a sound basis, but for the greater part of the nineteenth century the nomenclature of the papular eruptions of infancy and childhood remained confused. The same condition is often described under several different terms and the same term has been applied by various authors to apparently different conditions. By the end of the century greater uniformity of nomenclature had been achieved and the terms still employed by most British and American writers, papular urticaria and lichen urticatus, were regarded as synonyms. Strophulus is now generally regarded as synonymous with papular urticaria but even this name has been employed for other papular eruptions. In France strophulus or acute simple prurigo of Brocq are the terms in common use.

Jonathan Hutchinson (1879) emphasized the greatly increased frequency of papular urticaria in the summer months. Of 109 cases, 82 were seen between May and October, 27 between November and April. Adamson (1907) also noted that the peak incidence was between July and September. He found the sites most frequently affected to be the lumbar region, the buttocks, the outer sides of the arms and thighs and the wrists and hands. The papules succeeding the wheals are often surmounted by small vesicles and occasionally bullous lesions develop. Adamson noted the greater rarity of the severe forms in his better class patients. He gives the duration of the condition as a few days to two or three years.

Barber (1914) in an excellent clinical description emphasizes the tendency, which other authors had previously noted, for the lesions to appear in groups of six to 20 papules at intervals of two or three days. Tomkinson (1926) reporting on 102 cases seen in Glasgow merely confirmed earlier observations and noted that the sex incidence was equal.

Hallam (1927) published a careful study of 52 cases. The minimum age of onset was 3 weeks and the maximum 3 years, the average age at onset being just under 1 year. The eldest patient was aged 13 and had had the condition since the age of 1. Thirty-nine began in the summer months but 21 of these also had the eruption at times during the winter. The sites most favoured by the eruption were the buttocks, the lower third of the back, the thighs, ankles and forearms. In only two instances were two cases present in the same family. Thirty-one hospital admissions all resulted in rapid fading of

the eruption and no new lesions developed while the children were in hospital. The onset of the eruption in four cases coincided with removal to a new residence. One child was twice cleared of the eruption while on holiday. Corson, Perlman, Waltz and Ash (1931) investigating 31 cases in Philadelphia confirmed in general the work of other writers but did not agree in considering involvement of the face to be uncommon. Hallam (1932) published further clinical investigations. Eleven children were admitted to hospital for the nights only, spending the day at home. In eight no new lesions developed and in three cases a few sporadic papules appeared. Keeping the children in hospital by day only had no beneficial effect. Bringing the bedding from home to hospital led to the appearance of a few papules in one case on one occasion only. Hallam collected the incidence figures for papular urticaria in children under 14 in eight dermatological out-patient departments in London and provincial hospitals for the years 1927 to 1930. The figures ranged from 0·8% to 24% of out-patient attendances, the three London hospitals showing a notably high incidence. The annual incidence often showed striking variation from year to year, and in all the hospitals the incidence was exceptionally high in 1930.

Among Gordon's (1933) 50 cases more than one member of the family was affected in six instances. Onset or recurrence of the condition was noted to occur on returning home from hospital in 10 cases. Kinnear (1933) recorded the development of papular urticaria in 14 children aged 7 months to 9 years on arriving in this country from America. He confirmed that the eruption disappears when the child is admitted to hospital.

Pillsbury and Sternberg (1937) investigated 60 cases. They found that 80% developed below the age of 3. The sites involved in order of frequency were extensor forearms, the anterior surface of the upper arms and the back. Bray's (1937) observations on 200 cases agree in general but Bray considered that the face and other exposed parts were rarely involved.

Aetiology

The many aetiological hypotheses which have at one time or another found supporters can conveniently be considered under four main headings.

Digestive Disturbances and Food Allergy. Many of the earlier writers on papular urticaria attempted to relate the condition to digestive disturbances of various types and to dentition. As the concept of allergy developed during the first two decades of the present century the older theories were reclothed in new jargon and many investigations were undertaken employing new technical procedures.

Radcliffe Crocker (1903) believed that 'irritation of the alimentary canal' played an important role but Adamson (1907) was not satisfied with the current theory that digestive disturbances were responsible.

The authors who consider food allergy to be the cause of papular urticaria base their beliefs either on the results of skin testing or on the improvement of the condition on suppressing the foods considered to be responsible. Sidlick and Knowles (1922), using intradermal tests, found that nine of 12 children with papular urticaria reacted to one or more proteins. Three were cured when the incriminated foods were suppressed, four were improved and two were unimproved. This investigation was uncontrolled and it is not stated whether any of the children was admitted to hospital and, if so, whether readministration of the food in hospital reproduced the eruption. Corson *et al.* (1931) studied 31 cases and noted that the parents of the children were eager to incriminate foods in 23 cases. All skin tests were negative in 21 of the patients. In only one did elimination and readministration of a food substance apparently influence the eruption.

Walzer and Grolnick (1934) in a similar investigation found positive skin tests to one or more allergens in only nine of 36 cases of papular urticaria. Specific therapy as suggested by the skin tests was of no value. These authors consider papular urticaria to be an atopic disorder.

Neither Hallam (1927) nor Gordon (1933) was able to establish a dietary factor in any of their patients.

Pillsbury and Sternberg (1937) considered that the evidence in support of an allergic origin of papular urticaria was meagre. Bray (1937), however, strongly supported the relationship to food allergy. He considered that fats, especially pig products, fish, eggs and chocolate were frequently responsible, and he claimed to have produced new lesions within 24 hours of feeding a child with pork, ham or bacon, and suggested that the coexistence of a thermal factor was necessary to produce the skin lesions, and attempted to explain in this way the seasonal incidence and the frequent development of new lesions at night.

Tate (1935) investigated very thoroughly a series of cases of papular urticaria and gave a valuable review of the literature. He was unable to establish food sensitivity as a cause in any single case. He confirmed the observations of Hallam and others that the aetiological agent was connected with the patient's home environment and that it was not bedding or clothing although it could be carried on these articles. The incidence of a family history of

atopic disorders was no higher in his cases than in normal controls.

Urbach (1938) claimed that sensitivity to a food protein or occasionally a carbohydrate substance could be established as the cause of the eruption in 28% of his 225 cases.

Although food allergy is still widely accepted as a cause of papular urticaria it is impressive that there is no published series of cases that we can discover, with the possible exception of Urbach's, in which it has been claimed that administration of any food to a child in hospital under controlled conditions has ever provoked papular urticaria. Many of those who have investigated the problem most thoroughly have been able to convince themselves that food sensitivity plays no part whatever in this disease. The seasonal incidence, the striking variation in frequency from year to year and the complete immunity of the child in hospital cannot be accounted for on the basis of food allergy.

Nervous Factors. Gordon (1933) was impressed by the importance of psychological factors. Other authors have also raised this question but it has received little consideration in recent years. Winnicott (1934) considered that papular urticaria was a normal phenomenon of an erectile organ, a reaction to nervous stress or to external causes. Nervous stress can apparently heighten the reactivity of the skin but there is as yet no evidence that nervous factors play any part in papular urticaria.

Infection. Botter (1952) prepared a Seitz filtrate of the nasopharyngeal washings of four mothers whose children had papular urticaria. He dropped the filtrate into the nasopharynx of eight children who had recovered from papular urticaria and of one child with eczema. All the children developed an eruption 'resembling papular urticaria although the efflorescences were somewhat smaller, sometimes grouped and not as intensely itching as in the typical disease'. No virus could be demonstrated. This work obviously requires confirmation. If an infective agent is responsible for papular urticaria it is difficult to account for the complete lack of reports of contact cases when these children are admitted to hospital.

Parasites. Hutchinson (1879) wrote:

> 'Is it not very singular that one author after another who has looked carefully at the spots has been puzzled to tell whether they were bites or not? . . . My belief is that in very many cases the eruption is simply the result of flea bites on a pruriginous skin. . . . It is the fact that only in a few persons does the flea bite cause a wheal which misleads the nurse.'

Radcliffe Crocker (1903) wrote:

> 'Hutchinson considers this disease to be entirely due to flea and bug bites and the like in the first instance. I am convinced this is far too narrow a view and that, though true of many cases, among the poor especially, irritation of the alimentary canal plays quite as, or even more, important a role in children than in adults, to say nothing of the recognized causes of urticaria.'

The main objections raised to the parasitic origin of papular urticaria have been the relative infrequency with which more than one member of a family has been affected in most series of cases, the fact that new lesions did not develop when children slept in their own clothing and bedding in hospital (Hallam), and the apparent improbability of a parasitic origin in certain cases. Many authors have insisted on their own ability to differentiate insect bites from 'true papular urticaria'.

The parasitic theory had had few supporters in the two previous decades when Hamburger and Dietrich (1938) claimed that all or most cases of papular urticaria were due to insect bites. Many children are not sensitive to bed bug bites, but about a third develop a wheal and later a bulla if exposed to the bite. Two-thirds to three-quarters of children with papular urticaria, however, are sensitive to bed bug bites and the evolution of the bites is similar to the lesions of papular urticaria. Further investigations (Dietrich, 1938) showed that two-thirds of 50 children with papular urticaria were sensitive to bed bug bites and the remainder to flea bites. All cases were sensitive to one or the other and some were sensitive to both. Blank, Shaffer, Spencer and Marsh (1950) and Shaffer (1950) tested 30 children with papular urticaria with flea antigen and bed bug (cimex) antigen. Seventy-seven per cent. were sensitive to one or both, whereas only two of 124 controls were sensitive. Among 87 cases there was known exposure to fleas in 26 and to bed bugs in eight and possible exposure in 72. Eighty-eight cases were treated by conventional methods. Twenty-one per cent. were cured in an average of ten weeks. Fifty-four cases were treated with 5% D.D.T. in talc used as a dusting powder and their quarters were sprayed with 'flit' containing 5% D.D.T. Eighty-six per cent. were cured in two to three weeks. Blank and Shaffer point out that all the observed features of the natural history of papular urticaria are explained if the insect hypothesis is accepted.

Tate was one of the first to draw attention to the fact that the papular lesion is essentially different from true urticaria. A patient of his with papular urticaria developed a true urticaria due to fish sensitivity, the lesions consisting only of evanescent wheals. Histamine phosphate, 1 in 1,000, pricked into the skin of a child with papular urticaria produced only a transitory wheal as in normal

controls. Small pieces of nettle also produced whealing without papule formation. Cornbleet (1949) emphasized that the failure of papular urticaria to respond to antihistamines was further evidence that the reaction is of a special type. The observed lesions of papular urticaria with their biphasic course, initially urticarial and later papular, conform exactly with the known reaction to insect bites as established by Mellanby. Mellanby (1946) working with the yellow fever mosquito was able to show that subjects bitten for the first time develop an early erythematous macule followed after 24 to 48 hours by a papule. After repeated bites the immediate reaction was an urticarial wheal followed by a delayed papule. Later the delayed reaction disappeared and there was less itching and eventually, with complete desensitization, even the immediate reaction failed to appear. The length of time required for complete desensitization varied considerably from one individual to another. Rockwell and Johnson (1952) confirmed Mellanby's findings. They also were working with mosquitoes. Two of their patients had been diagnosed as papular urticaria by dermatologists.

These important observations not only offer an explanation for the type of lesion observed in papular urticaria but also explain such observations as those of Kinnear, already quoted, and other observations, including our own, in which individuals exposed to a new environment develop papular urticaria. Gordon (1950) showed experimentally that some individuals develop no reaction to insect bites. Taken in conjunction with Mellanby's work Gordon's results account both for the fact that only a small proportion of those exposed to the insects may develop papular urticaria and for the spontaneous cure of the condition after a variable duration in the majority of cases. The occasional persistence of papular urticaria into adult life is accounted for by the occasional failure of desensitization as noted by Mellanby. Shaffer, Jacobson and Pori (1952) consider that the evidence in favour of insect bites as the cause of papular urticaria is strong as it is based on the combined results of studies on different aspects of the problem, clinical epidemiological, allergic (skin tests), histological and therapeutic. The similarity of the course of experimental sensitivity to insects and natural papular urticaria is striking.

Life Histories of Fleas and Bed Bugs. Many of the difficulties which some authors have felt in accepting the parasitic aetiology of papular urticaria are readily explained when the life histories of fleas and bed bugs are studied (Herms, 1950). The eggs of the human flea, *Pulex irritans*, and the cat and dog fleas, *Ctenocephalides felis* and *canis*, are laid in the nests or sleeping quarters of their hosts. They are dry and do not remain attached to the hosts' hairs. Eggs are usually laid in warm weather, particularly when the humidity is high, and the incubation period, which varies from two to 12 days, is shortest under these optimum conditions. The larval stage lasts from nine to over 200 days depending on whether conditions are favourable. The larvae can be found in the crevices of floors and under carpets or in kennels. They can survive with little or no food. The length of the pupal period also varies with the temperature and is between seven and 300 days. The adult fleas visit the host only for short periods for feeding and can remain for many months without food. The host specificity of fleas is not well marked and these three species will all freely bite man. The fact that fleas visit their hosts only for a few minutes at intervals of two or three days in order to feed explains both the failure of Hallam's experiments with clothing and bedding and also the liability for new lesions of papular urticaria to develop at night and at short, irregular intervals. The maximum incidence of papular urticaria in the warm, moist months of the year coincides with the season of maximum prevalence of fleas.

The bed bug, *Cimex lenticularis*, lays its eggs on rough surfaces, in cracks and crevices and behind woodwork or wallpaper. The eggs are attached by a quick drying cement and may therefore require stiff brushing to remove them. In warm weather the adult may lay two to three eggs daily but in spring and autumn, when the temperature is lower, the frequency of egg laying is considerably reduced. The eggs do not survive longer than three months in uninhabited houses. After hatching the nymph can live for three or four months at low temperatures without food but further development cannot occur. If food is available the nymph moults five times before reaching full adult development. An average time of 10 weeks is required from egg to adult.

The adult bed bug is a flat, oval insect one-fifth of an inch long and one-eighth of an inch broad. Its colour may be light or dark brown but after feeding is usually purple or red. It is chiefly nocturnal but will feed in the day time if conditions are favourable, and is said to be most active just before dawn. Under ideal conditions of temperature feeding takes place about once a week but in colder weather the frequency is reduced. The time required for feeding varies from five to 12 minutes after which the insect leaves its victim as fast as possible. The adult bed bug has been known to survive a year without feeding and for as long as four years with

occasional feeds. The temperature of the house is likely to have a considerable effect on the breeding of the bugs. If the temperature never falls below 55° F. for more than a few hours during the winter as, for example, in a bed-sitting-room, feeding and breeding will continue throughout the year. If the room is without artificial heat breeding will cease and feeding will become very infrequent during the winter. The bed bug is capable of travelling long distances in search of food, even from one house to another. The temporary storage of furniture, the purchase of secondhand furniture or its carriage in an infected van are all potential sources of infestation. The percentage of houses infested with bed bugs is highest in large cities, and, despite the efficacy of modern methods of control, bed bug infestation is still common.

Personal Cases

For the purpose of this article we have studied a series of 100 consecutive cases. The sexes were equally affected. The minimum age of onset was two weeks (papular urticaria developed within 24 hours of returning from the maternity home) and the maximum seven years; the average age of onset was 1 year and 10 months, 89% of our cases being under 3. Reliable information regarding seasonal incidence was available in 61 cases. Of these 62·3% were affected more severely in the summer and 9·2% in the winter. The remaining 29·5% were equally affected throughout the year. The distribution of the lesions was accurately recorded in 75 cases. In the majority the legs and the lower trunk were principally involved. The face was involved in 5·8%. All these findings are in general agreement with those of other authors. Some authors have, however, been impressed by the rarity with which other members of a family were similarly affected. Special inquiry on this point was made in 85 cases and in no fewer than 31·7% was another member of the family similarly affected. Since 21% of these cases were in only children, approximately 50% of the families in which there were other children at risk had one or more of these affected. In many families the children were affected in succession, rather than simultaneously, and frequently older siblings were stated to have suffered from 'heat bumps' at about the same age as the patient. In many families, however, the children were affected simultaneously.

In all cases the characteristic irregular grouping of the papules was noted and in several cases the lesions were grouped above or below the sites of pressure of elastic or other constrictions of underclothing or pyjamas, the actual site of constriction being free. The eruption was sometimes profuse and involved the greater part of the trunk and limbs conforming precisely with the classical conception of severe papular urticaria. In a few cases only two or three groups of papules were present and the diagnosis of insect bites would have been accepted without hesitation. Often a circumscribed and a profuse eruption were seen in different members of a family at the same time or in the same child at different times. We were able to confirm the constancy with which the lesions disappear when the child is admitted to hospital. The child remains clear while in hospital and quite regularly presents himself at the out-patient department with a new crop of lesions within a short time of returning home.

Blank *et al.* (1950) tried to assess the percentage of the children exposed to fleas or bed bugs. After careful study of the life histories of these insects we came to the conclusion that it is very seldom possible completely to exclude exposure to one or other of them. There were pets (cats or dogs) in the homes of 43 of the 51 children whose parents were specifically questioned on this point, but these figures have little value as no control figures are available. Moreover, many other parents mentioned that neighbours' pets were frequently in the house. Bed bug infestation is still relatively common in urban areas. In many cases, including some of those we have cited, the time of onset of the urticaria coincided too closely with the arrival of a new pet for this source of infestation to be ignored, but in the majority of cases precise data were almost impossible to obtain and unless the child is actually in hospital exposure to parasites can rarely be excluded with certainty.

We experienced similar difficulty in assessing the response to treatment. In some cases the response to the use of 5% D.D.T. in talc as a dusting powder was quite dramatic. In others dusting powder produced only a partial cure and in a few it was of no benefit. In some of the latter we were able to establish that the patients did not carry out our instructions. In some cases the removal or treatment of pets produced an immediate cure. The following cases are representative of the whole series:

Case 10. A boy aged 2½ years developed papular urticaria at the age of 18 months, his sister being first affected at the same time. Both children cleared simultaneously when their family moved from the home of an aunt with whom they had been living since the onset of the condition.

Case 12. A small boy aged 2½ together with his sister suffered from attacks of papular urticaria from October, 1951, until January, 1952. When the children were last seen in August, 1952, neither had had any new lesions since January. No treatment had been given and no dietary restrictions imposed, the only variable factor

being the presence of the cat which was purchased in October, 1951, was lost in January, 1952, and did not return.

Case 15. A girl aged 3, had lived in Durham up to the age of 18 months. She developed urticaria within a few weeks of the family moving to Cardiff and attacks have occurred at intervals since.

Case 20. A boy aged 2½ had been living in Birmingham until two weeks before he was first seen. The day after his arrival in Cardiff he developed extensive papular urticaria which became secondarily infected. He was admitted to hospital and developed no fresh lesions. During the time he was in hospital his sister continued to attend the out-patient department with repeated crops of new lesions. This boy had had a similar short attack whilst staying with his grandmother in Cardiff at the age of 6 months. It had cleared immediately when he returned to his home in Birmingham.

Case 29. A small girl aged 5, together with her brother, suffered from attacks of papular urticaria which regularly coincided with visits to her grandmother. The attacks started at the age of 1. Another grandchild, usually living in Germany and never previously affected, also developed papular urticaria whilst spending a holiday with the grandmother.

Case 41. A brother and sister aged 2½ and 1: the boy who had lived since birth in Stoke, was seen with a characteristic attack of papular urticaria which had developed within 48 hours of his arrival in his grandmother's home in Cardiff. His only previous attack was during an earlier holiday visit to his grandmother at the age of 6 months. His small sister visiting Cardiff for the first time was similarly affected.

Case 73. A girl aged 2 had had extensive lesions for two months. Her skin cleared completely during 10 days in hospital and no new lesions developed. The eruption recurred when she returned home.

Case 87. A boy aged 5 had had papular urticaria continuously from the age of 9 months. He developed no new lesions during the week in hospital but the condition recurred when he returned home.

Discussion

Lever (1952) contributing to the latest edition of an authoritative textbook on paediatrics writes very briefly on papular urticaria that 'the cause of the disease is hypersensitivity to insect bites, especially to the bites of bed bugs and fleas'. A review of the literature quickly establishes that the majority of the hypotheses which have at one time or another been put forward can no longer be supported. Study of our own cases is somewhat inconclusive, but we were impressed by the fact that the clinical picture and course of those cases, which seem beyond any possible doubt to be attributable to hypersensitivity to insect bites, differ in no single respect from those cases in which the circumstantial evidence was rather weaker. Although Lever's dogmatism is probably fully justified we feel that on present evidence we can merely claim that sensitivity to insect bites appears to be the cause of the majority and possibly all the cases of papular urticaria we have encountered in South Wales. The possibility that papular urticaria is a syndrome with multiple causes cannot be completely excluded but we found no evidence of any other cause in our own cases and we know of no convincing evidence in the literature that any other cause has ever been reliably established. We would suggest that although the case cannot be considered conclusively proved the physician confronted with a child with papular urticaria is at least under an obligation to employ every available means to exclude a parasitic origin before subjecting the child to any other investigations. Dietary restrictions can no longer be justified.

Treatment

If papular urticaria be accepted as of parasitic origin a complete revision of conventional treatment naturally follows.

Disinfestation. Careful enquiry will frequently establish the probable nature and source of the infestation and appropriate measures can be adopted to control it. Even when the source of the infestation is not apparent from the history the empirical use of a disinfestation routine can sometimes produce a dramatic and satisfactory cure. Control measures should always be planned after careful consideration of the natural history of the pests. For example, the removal or disinfestation of domestic pets cannot always be relied on as fleas can survive in and around the sleeping quarters and may attack the child, the alternative host, with increased vigour when the natural host is removed. Recent progress in insecticides has been reviewed by Brown (1951) and in a symposium arranged by Buxton (1952). Tentatively, the following simple measures are recommended:—

Fleas. Treat the animals' sleeping quarters with a 5% D.D.T. spray in kerosene, paying special attention to bedding, floor coverings and crevices. Dust dogs with 5% D.D.T. powder. For cats 'rotenone' or pyrethrum powder is to be preferred as cats may lick their fur and D.D.T. may prove toxic.

Bed Bugs. Treat floor coverings, floor boards, skirting and furniture with 5% D.D.T. in kerosene. Residual toxicity is said to persist for nearly 200 days.

Symptomatic Treatment. In the majority of cases if disinfestation is carried out promptly and efficiently calamine lotion and simple sedation with phenobarbitone for a few nights are all that is required. We have not found the antihistamines effective. Where bullous lesions have become secondarily infected antibiotics systemically or locally may be

indicated. Occasionally when the eruption is exceptionally profuse and of long duration the child may have lost weight as a result of lack of sleep and perhaps unnecessary dietary restrictions. In these cases admission to hospital for a few days may be desirable as it not only establishes the parasitic origin of the eruption beyond doubt but allows time for thorough disinfestation before the child returns home. Eder (1945) claimed that thiamine chloride in a dose of 30 mg. daily for three days and 10 mg. daily for six weeks gave infants complete protection against flea bites. A limited experience of this procedure has not given encouraging results.

It occasionally happens in cases where there is strong circumstantial evidence incriminating flea or bed bug bites that disinfestation is difficult to carry out effectively or is even quite impracticable. In such cases desensitization deserves consideration but we have had no personal experience of it.

Summary

After reviewing the literature and investigating a series of 100 cases of papular urticaria we consider that there is strong evidence that most, if not all cases, of papular urticaria are the result of an acquired sensitivity to the bites of certain insects, particularly fleas and bed bugs. Provisionally accepting the validity of this hypothesis recommendations for treatment are outlined.

References

Adamson, H. G. (1907). *The Skin Affections of Childhood*, p. 255. London.
Barber, H. W. (1914). *Practitioner*, **93**, 820.
Bateman, T. (1813). *A Practical Synopsis of Cutaneous Diseases*, 2nd edit., p. 13. London.
Blank, H., Shaffer, B., Spencer, M. C. and Marsh, W. C. (1950). *Pediatrics*, **5**, 408.
Botter, A. A. (1952). *Dermatologica, Basel*, **104**, 87.
Bray, G. W. (1937). *Recent Advances in Allergy*, 3rd edit., p. 365. London.
Brown, A. W. A. (1951). *Insect Control by Chemicals*. New York and London.
Buxton, P. A. (1952). *Trans. roy. Soc. trop. Med.*, **46**, 213.
Cornbleet, T. (1949). *Arch. Derm. Syph., Chicago*, **60**, 1167.
Corson, E. F., Perlman, H. H., Waltz, A. D. and Ash, R. (1931). *Arch. Pediat.*, **48**, 349.
Crocker, H. Radcliffe (1903). *Diseases of the Skin*, vol. 1, 3rd edit., p. 120. London.
Dietrich (1938). *Mschr. Kinderheilk.*, **75**, 70.
Eder, H. L. (1945). *Arch. Pediat.*, **62**, 300.
Gordon, H. (1933). *Lancet*, **2**, 126.
Gordon, R. M. (1950). *Brit. med. J.*, **2**, 310.
Hallam, R. (1927). *Brit. J. Derm.*, **39**, 95.
—— (1932). *Ibid.*, **44**, 117.
Hamburger, F. and Dietrich (1937). *Acta paediat., Uppsala*, **22**, 420.
Herms, W. B. (1950). *Medical Entomology*, 4th edit., p. 419. New York.
Hutchinson, J. (1879). *Lectures on Clinical Surgery*, vol. 1. London.
Kinnear, J. (1933). *Brit. J. Derm.*, **45**, 65.
Lever, W. F. (1952). *The Child in Health and Disease*. Ed. C. G. Grulee and R. C. Eley. 2nd edit., p. 986. London.
Mellanby, K. (1946). *Nature Lond.*, **158**, 554.
Pillsbury, D. M. and Sternberg, T. H. (1937). *Amer. J. Dis. Child.*, **53**, 1209.
Rockwell, E. M. and Johnson, P. (1952). *J. invest. Derm.*, **19**, 137.
Sidlick, D. M. and Knowles, F. C. (1922). *Amer. J. Dis. Child.*, **23**, 316.
Shaffer, B. (1950). *Arch. Derm. Syph., Chicago*, **62**, 259.
——, Jacobson, C. and Pori, P. P. (1952). *Ann. Allergy*, **10**, 411.
Tate, B. C. (1935). *Archives of Disease in Childhood*, **10**, 27.
Tomkinson, J. G. (1926). *Brit. J. Derm.*, **38**, 431.
Urbach, E. (1938). *Derm. Z.*, **78**, 77.
Walzer, A. and Grolnick, M. (1934). *J. Allergy*, **5**, 240.
Winnicott, D. W. (1934). *Brit. J. Child. Dis.*, **31**, 5.

FOETAL VACCINIA

BY

A. M. MACDONALD and P. MACARTHUR

The Royal Hospital for Sick Children, Glasgow

(RECEIVED FOR PUBLICATION APRIL 27, 1953)

This paper presents a case of vaccinial infection in the foetus, the second known to have occurred.

Generalized vaccinia in the foetus has been recognized only once before. Lynch (1932) described a prematurely born child showing clinical and pathological features very similar to the present case. Lynch made a thorough survey of the literature on foetal skin disease, especially on foetal variola, in order to establish his diagnosis of foetal vaccinia. He discovered 47 reports of variola in the foetus but no previous instance in which vaccinia was recognized. Others (Vignes, 1942) also failed to find any report of foetal vaccinia, and Ballantyne (1902) in his classical monograph on foetal disease stated that 'an infant has never been born carrying a vaccination pustule upon its skin, as a result of the vaccination of the mother'. We have been unable to trace any record of a case of foetal vaccinia since Lynch's report.

Lynch quoted 11 reports of single cases described as foetal variola without variola in the mother, including one by Jenner. In three of the reports the author did not state that the mother had been in contact with a case of smallpox. In none of the cases was the possibility considered that the foetal disease might be due to vaccinia though in several it was mentioned that the mother was recently vaccinated. It seems possible that at least some of these may have been unrecognized instances of foetal vaccinia.

Clinical Record

Between March 26 and April 1, 1950, 18 cases of smallpox occurred in the vicinity of Glasgow. This outbreak caused considerable alarm among the local population and in consequence nearly half a million people were vaccinated during the first three weeks of April (Laidlaw and Horne, 1950). One of these was an unmarried woman aged 19 years who was working on a farm in Lanarkshire. She was about three months pregnant at the time of vaccination and she had never been vaccinated before. She developed a severe primary vaccination reaction with a large area of redness and induration and with considerable general upset of health so that she could not do her work for two or three days. Eleven weeks later she was spontaneously delivered of a live premature infant, who was thus of about six months' gestation.

She had given birth to a normal healthy child 18 months before the present child was born. With the exception of the vaccination reaction she had been perfectly well during the pregnancy and she had a normal puerperium without fever or abnormal lochia. After delivery she and her child were admitted to Strathclyde Infectious Diseases Hospital, Motherwell, where her blood Wassermann reaction was found to be negative; a blood culture was sterile, and a blood white cell count was normal.

The child was examined three and a half hours after delivery. He was a cold, hydropic premature infant and was whining feebly. About 25% of the body surface was covered with multiple, discrete and confluent, circular and umbilicated, greyish white, sodden lesions, with no surrounding erythema. The child's blood was sterile on culture and blood Wassermann and Kahn reactions were negative. He died 15 hours after birth.

Necropsy Findings

A necropsy was performed five hours after death. The body was that of a premature male infant weighing 1,090 g. and estimated to be under seven months' gestation. The skin lesions were extensive. That over the left side of the face was circular, centred at the inner third of the zygomatic arch and extending anteriorly to the middle of the eyelids on that side and posteriorly to the pinna and tragus. The edges were scalloped and raised. The skin of the lesion was light in colour and necrotic. Underneath it was some caseous material on a granulation foundation. The necrotic part was easily removed. Similar lesions were seen on the outer aspects of both arms and to a lesser extent on the forearms. There was a small patch on the upper inner aspect of the right thigh and a large asymmetrical lesion covered most of the back from the neck to the level of the first lumbar spine. Smaller oval lesions were present over the epigastrium and in the midline of the abdomen above the umbilicus. There were no lesions

FIG. 1.—Frontal view of infant showing the cutaneous lesions.

FIG. 2.—Back view to show the greater extent of the cutaneous lesion when compared to the front.

on the palms or soles or round the anus (Figs. 1 and 2).

Many blocks from the skin were made and cut. There was massive necrotic cellulitis with some fibrosis in the corium and re-epithelialization at the centre of the lesion (Fig. 3). Most of the deeper necrotic foci were strikingly limited to the hair follicles (Figs. 4 and 5). The skin epithelium was either completely denuded or thickened with long prolongations into the corium. The cellular reaction was mainly mononuclear in type similar to that seen in other virus infections, but large numbers of eosinophils were also seen. No bacteria were observed in Gram-stained sections. Tissue stained for virus bodies by Lendrum's (1947) phloxin-tartrazine method showed highly refractile eosinophil inclusion bodies (Fig. 6). The umbilical cord was attached and healthy and histologically normal.

The brain was primitive. No gyri had been formed and its total weight was 123 g. There was an extensive ventricular haemorrhage which had originated from the veins lying between the thalamus and the lentiform nucleus. A block was made from the cerebral hemisphere including the middle part of the ventricle and others from the thalamus, pons, cerebellum and medulla. Sections from these showed normally developing brain and no virus bodies were detected.

The mouth was clean and the larynx and trachea were normal. The lungs were poorly expanded and the pleural surfaces were normal. On cutting the right lung a firm white area, 1 cm. in diameter with an indefinite margin, was found in the lower lobe posteriorly, and next to it beside a small bronchus was a smaller red focus. Elsewhere no lesion was found. Histologically there was considerable atelectasis and many alveoli contained amniotic debris and so-called vernix membranes. Next to a small bronchus there was a lesion with a massive necrotic centre, in which calcium could be demonstrated by Von Kossa's method, bounded by granulation tissue (Fig. 7). No bacteria were seen in sections stained by Gram's and Ziehl Neelsen's methods. Lendrum's phloxin-tartrazine method showed aggregations of virus particles identical with those seen in the skin.

The thymus appeared normal to the naked eye but microscopically large numbers of eosinophils were seen mainly in the connective tissue septa. The heart was normal, weighing 5 g., and its histology was normal. The oesophagus, stomach and intestines presented no abnormality but there was a moderate infiltration of eosinophils into the epithelium of the colon. The spleen weighed 6 g. and the liver 70 g.; they were within normal limits of size, shape and colour, and both of these organs histologically presented a picture of extensive haemopoiesis compatible with the age of the foetus. No virus bodies were recognized. The gall bladder and ducts were normal. The adrenals were normal. The pancreas appeared normal; histologically, haemopoiesis was present and the impression was formed that eosinophil myelocytes were relatively increased. The kidneys were of equal size weighing 11 g. together. No lesion was seen by the naked eye, and histologically there was extensive haemopoiesis. A section through the end of a rib showed normally developing bone and marrow.

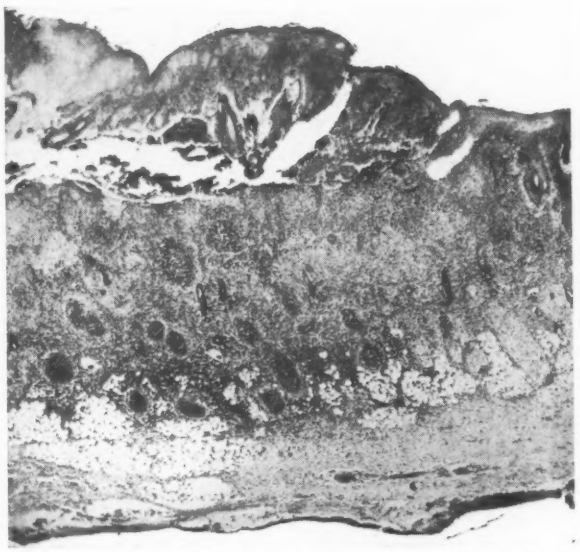


FIG. 3.—Section of skin lesion to show the necrotic cellulitis, re-epithelialization at the centre of the lesion and the necrosis of the hair follicles. Haemotoxylin and eosin ×20.

Discussion

It is claimed that the clinical and pathological features in this case justify the diagnosis of generalized foetal vaccina. The mother is known to have reacted strongly to the vaccination and the systemic upset must have been considerable to force her to take to bed in the spring-time, because she was a strong, healthy woman employed as a farm labourer. She bore a large recent vaccination scar on the left shoulder.

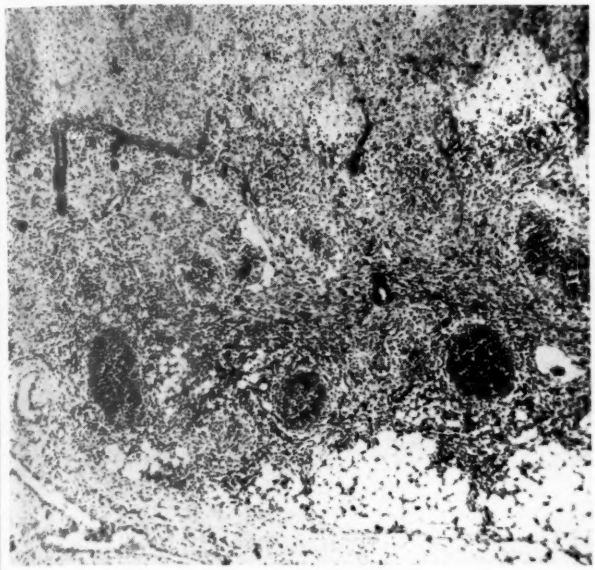


FIG. 4.—Higher power view of the corium to demonstrate the surface necrosis and the hair follicle lesion with early re-epithelialization. Haematoxylin and eosin ×40.

Successful vaccination is accompanied by viraemia and from this woman the infection must have spread to the foetus in one of four ways: first, directly from the maternal bloodstream to the foetus by traversing the placental barrier. It has often been claimed that if a woman is vaccinated late in pregnancy she may transmit a certain amount of immunity to her child and many children born to such mothers cannot be successfully vaccinated, or give an immune response when vaccination is attempted during the neonatal period (Ballantyne, 1902). If it is accepted that in vaccinia the foetus may develop active immunity *in utero*, the foetus must be invaded by the virus about the same time as the maternal viraemia or it would become immune with the mother and therefore very unlikely to suffer disease if later attacked by the virus. Much depends on whether maternal immunity to vaccinia is transferred to the foetus or is not; unfortunately published opinion is divided on this point. It cannot be assumed that once foetal infection has occurred the incubation period of the transplacental infection is the same as that which follows inoculation of the skin. Mothers with variola have been delivered of children with a typical variola rash

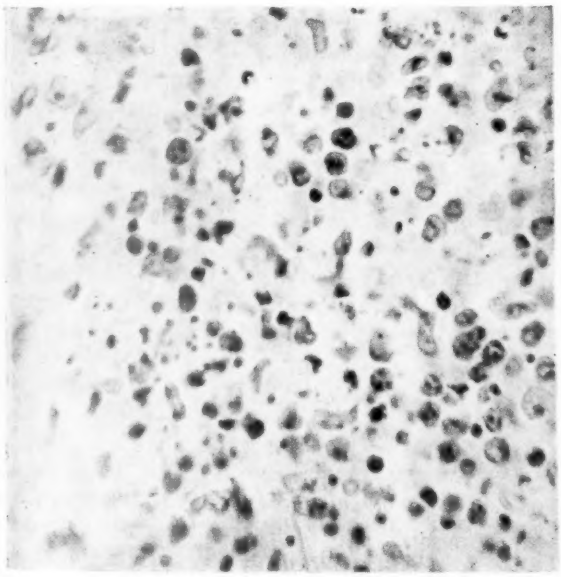


FIG. 5.—A hair follicle, to show the necrosis and the surrounding cellular reaction including many eosinophils. Haematoxylin and eosin ×150.

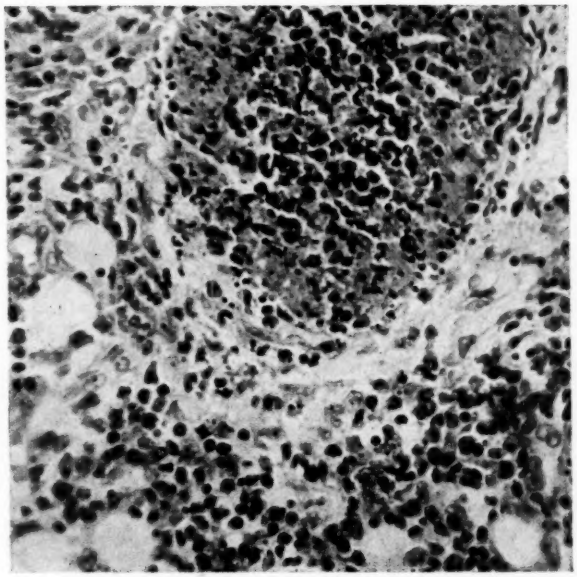


FIG. 6.—The inclusion bodies in the corium with the type of cellular reaction associated with them. An identical picture was seen in the tissue surrounding the lesion of the lung. Phloxin-tartrazine ×400.

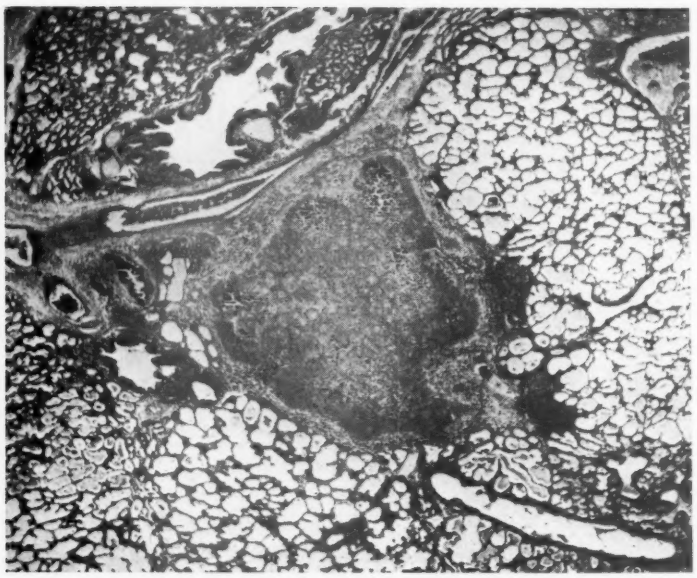


FIG. 7.—Low power view of lung lesion. Even with this stain the presence of calcium can be detected. Haematoxylin and eosin × 20.

at periods ranging from two weeks to three months after the maternal eruption and the same may well occur in vaccinia.

Second, maternal viraemia may have led to a metastatic lesion or lesions in the placenta and subsequent invasion of the foetus from this lesion. The foetal disease would then occur later than the maternal infection and it thus must be assumed that the foetus did not acquire immunity synchronously with the mother's immunity.

Third, the placenta and the membranes could develop a general infection, like the allantoic sac of an experimentally infected fertile hen's egg, bathing the foetal skin with infected amniotic fluid. There is no evidence that this did occur because unfortunately the placenta and membranes were not seen and could not be obtained for examination. Nevertheless there is indirect evidence that tends to favour this hypothesis. The skin lesions are very irregularly distributed but are most widespread on the extensor surfaces where the massage effect is greatest and the inflammatory reaction is maximal at the roots of the hair follicles in the corium, possibly indicating that the virus entered through these channels from the surface of the body by a means similar to inunction. Furthermore it seems possible that the lesion in the lung is not blood-borne but due to direct contact with the infected amniotic fluid during foetal respiratory movements. However, Professor A. W. Downie kindly drew our attention to the magnificently illustrated monograph of Ricketts and Byles (1908) in which the effect of mechanical trauma to the skin during the incubation period of smallpox has been extensively studied and depicted. These authors show that in smallpox mild irritation of the skin can determine the site of a very profuse crop of lesions or even a confluent patch. It may be that this factor determined the irregular distribution of the lesions in the present case.

The fourth hypothesis is purely conjectural and is put forward for completeness and because it might help to explain why generalized foetal vaccinia is such a rare condition though there must have been many women who were vaccinated during pregnancy. The woman was about three months pregnant when vaccinated. She was unmarried. She had already one other child to provide for. Presumably this pregnancy was unintentional and the child unwanted. Furthermore during the period of viraemia she was ill, unfit for work, and probably depressed. It is possible that she attempted abortion at this time, and by damaging her own tissues opened up blood vessels which transmitted the virus in her blood to the amniotic cavity. If this series of events occurred the condition described in our second hypothesis could occur but synchronously with the maternal viraemia and before the foetus could have acquired immunity from the mother.

The time factor is difficult to assess. The granulations of the skin had been present for a period of weeks and the time required for calcium to form in the lungs may be estimated in similar units. Inclusion bodies were not found in any tissues other than the skin and lungs. We believe that the infection of the foetus may have come from infected amniotic fluid, but in the absence of the placenta and membranes final proof of this is lacking. The rarity of the condition may be due to the sequence of events in our fourth hypothesis or it may be that abortion normally follows in almost all cases where vaccination of the pregnant woman leads to viraemia in the foetus.

Summary

A description is given of the clinical and pathological findings in a premature infant born three months after the primary vaccination of the mother. It is claimed that the child was infected with the virus of vaccinia *in utero* and was born suffering from generalized congenital vaccinia. Previous reports of a similar condition were sought and only one other example of the disease has been found.

The pathogenesis of the condition is discussed in the light of the present case and the rarity of this complication of vaccination is emphasized.

We wish to thank Dr. G. B. S. Roberts for the preparation of the sections demonstrating virus aggregations and Dr. R. S. Dewar for permission to report the blood cultures and Wassermann reactions done in Strathclyde Hospital.

REFERENCES

Ballantyne, J. W. (1902). *Manual of Antenatal Pathology and Hygiene —The Foetus.* Edinburgh.
Laidlaw, S. I. A. and Horne, W. A. (1950). *Med. Offr.*, **83**, 187.
Lendrum, A. C. (1947). *J. Path. Bact.*, **59**, 399.
Lynch, F. W. (1932). *Arch. Derm. Syph., Chicago*, **26**, 997.
Ricketts, T. F. and Byles, J. B. (1908). *The Diagnosis of Smallpox.* London.
Vignes, H. (1942). *Presse méd.*, **50**, 364.

E.E.G. FINDINGS IN 100 CASES OF SEVERE ENURESIS

BY

E. C. TURTON and A. B. SPEAR

From the Department of Electro-encephalography and Electro-Physiology, Barrow Hospital, Nr Bristol

(RECEIVED FOR PUBLICATION MARCH 10, 1953)

The purpose of this paper is to describe one aspect only, namely the electro-encephalographic, of the perennial problem of enuresis.

One hundred children and adolescents with severe enuresis and without any discoverable organic condition were investigated. All suffered from nocturnal enuresis but a considerable proportion were wet during the day as well. Sixteen had had a dry period of varying duration, the remainder having been persistently enuretic from birth. Encopresis was noted in addition in four cases. Apart from ordinary physical examination and urine testing, the majority had had extensive investigations, e.g., intravenous pyelograms and cystometrograms. The sample does not represent a fair cross-section of children and adolescents suffering from enuresis as the ones who had been amenable to simple treatment did not as a rule reach us, so that there was a heavy loading in favour of the more severe type of case. No children were included who were mentally defective or markedly backward, nor where there was any clinical history of epilepsy, 'fits' or attacks of unconsciousness. The sex distribution showed a preponderance of males, as was to be expected, with 63 boys and 37 girls. No child was included under the age of 5 and the age distribution was as shown in Fig. 1.

Procedure

Care was taken to reassure the children about the examination. No tracings were included which were technically unsatisfactory owing to the child being uncooperative. Recording was undertaken in most cases soon after a meal but in a small minority after the ingestion of glucose.

Records were taken mainly on an 8-channel 'ediswan' electro-encephalograph but with some on a 6-channel machine from the same makers. The machines were linked to automatic low frequency wave analysers which were used routinely. After recording from standard electrode positions over-ventilation was performed vigorously for two to three minutes in 75 cases. In the remaining 25 it was only poorly practised. After a further period of record taken at rest, photic stimulation was applied both as 'free flicker' and with an electronic trigger mechanism (Hewlett, 1951; Turton, 1952).

Criteria Adopted

The evaluation of children's records presents far greater problems than in the case of adults. There is considerable difference of opinion between various centres as to what constitutes a normal record for any given age. Earlier workers undoubtedly did not allow sufficiently for the wide variation in records taken from apparently normal children of the same age group. For instance, Smith (1938) found a well developed alpha rhythm in most children by the age of 3. Lindsley (1939) at 5 years found an

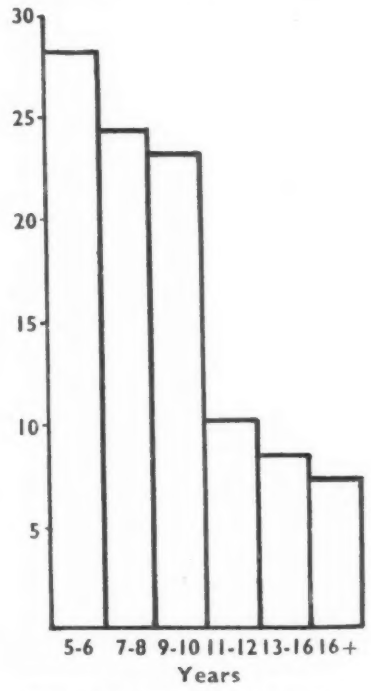


FIG. 1.—Age distribution of the series.

average frequency of 8·4 c.p.s. with a range only between 7·3 and 9·4 c.p.s. Similarly Brill and Seidemann (1941) found very little scatter in the alpha frequency of 100 normal children from 4 to 15 years. Gibbs and Gibbs (1941) give examples of normal and questionably normal records. Jasper (1949) quoting Bernhard and Skoglund stresses that the increase in the dominant E.E.G. frequency with age approximates to a logarithmic curve in common with many growth processes. Once again the rhythms increased rapidly in frequency to the age of 5 and remained relatively static from 5 to 10 years with a dominant alpha rhythm.

Henry (1944), in a large scale survey, in addition to studying alpha development paid attention to the incidence of slower activity in children of 6 years and over, and was surprised at the amount which he found. Walter (1950) gives valuable criteria of normality and stresses the wide variation in each age group. Pond (1951) strikes a similar warning note.

Our own concept of normality was to some extent influenced by the literature, but it was strongly felt that many of the earlier papers provided too rigid criteria. Hence, as a result of our own experience and the more recent studies mentioned above, we have tried to err on the side of caution and have disregarded many minor deviations from the so-called normal.

In the age group 5-6 years marked theta activity was regarded as normal, but a persistent and dominant delta rhythm of high voltage combined with an absence of alpha and theta at 6 to 7 c.p.s. was considered to be immature. In the next age group, 7-8 years, these criteria also held true except that in some of those records considered abnormal there was an alpha component revealed by analysis but not readily visible in the primary trace. In the other age groups the same principles were applied but to a lessening degree.

No attention was paid to rhythmic delta and theta discharges evoked by over-breathing provided they did not persist for more than half a minute after cessation. Of those performing satisfactorily, 34 showed no significant alteration and these were principally aged 11 and over. Forty-one showed rhythmic slow discharges and in 21 the responses persisted after termination but for not longer than 30 seconds.

In childhood failure of the cortical rhythms to follow or respond to photic stimulation and the paucity of the evoked responses has been noted by Walter and Walter (1949). Our results show a steady increase of evoked responses with advancing age. Fig. 2 shows the number of children on whom photic stimulation had no apparent effect on the record. This was not considered abnormal. The electronic trigger mechanism produced similar results.

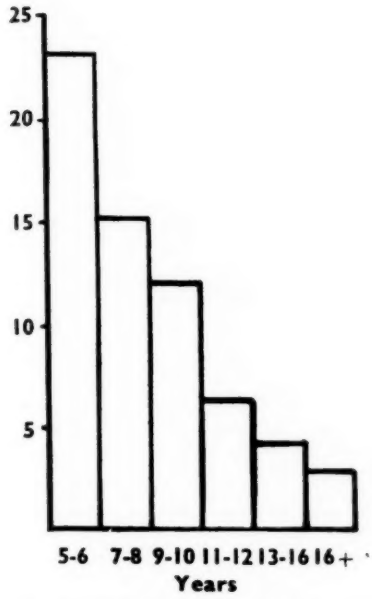


FIG. 2.—Diagram showing patients who did not respond to photic stimulation.

Results

Forty-nine per cent showed records which were normal or borderline normal. In the former category were all the records, 26, that gave rise to no serious doubts in classification. Seven cases showed mild epileptiform features but these were only of a rather dubious nature and it was felt safer to classify them as borderline normal. The remaining 16 of this group showed an excess of slow activity but as these were principally between the ages of 5 and 7 it was felt wiser to include them also among the borderline normals.

In eight cases abnormalities of an epileptiform nature were pronounced and the records were considered to be definitely abnormal but sustained seizure patterns did not occur. Fig. 3 shows such a record taken from a boy aged 14. In a further 14 the records were considered pathognomonic of epilepsy. Eight of these showed a resting record with seizure patterns and in the remaining six these occurred only when activation procedures were employed. Fig. 4 shows seizure patterns occurring in a 9-year-old girl during photic stimulation. Two showed a focus in the left temporal lobe. A definite excess of slow activity above that to be expected for their age was found in 28 cases. In all of these this

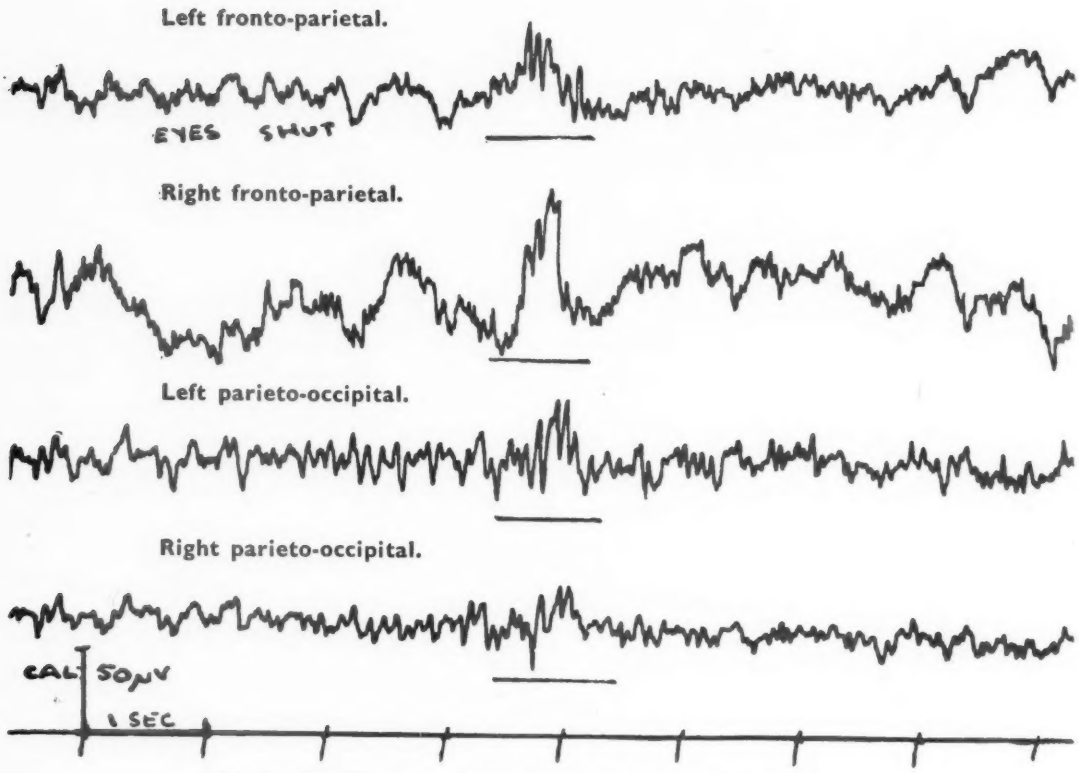


FIG. 3.—Epileptiform record from boy aged 14 with paroxysmal discharges.

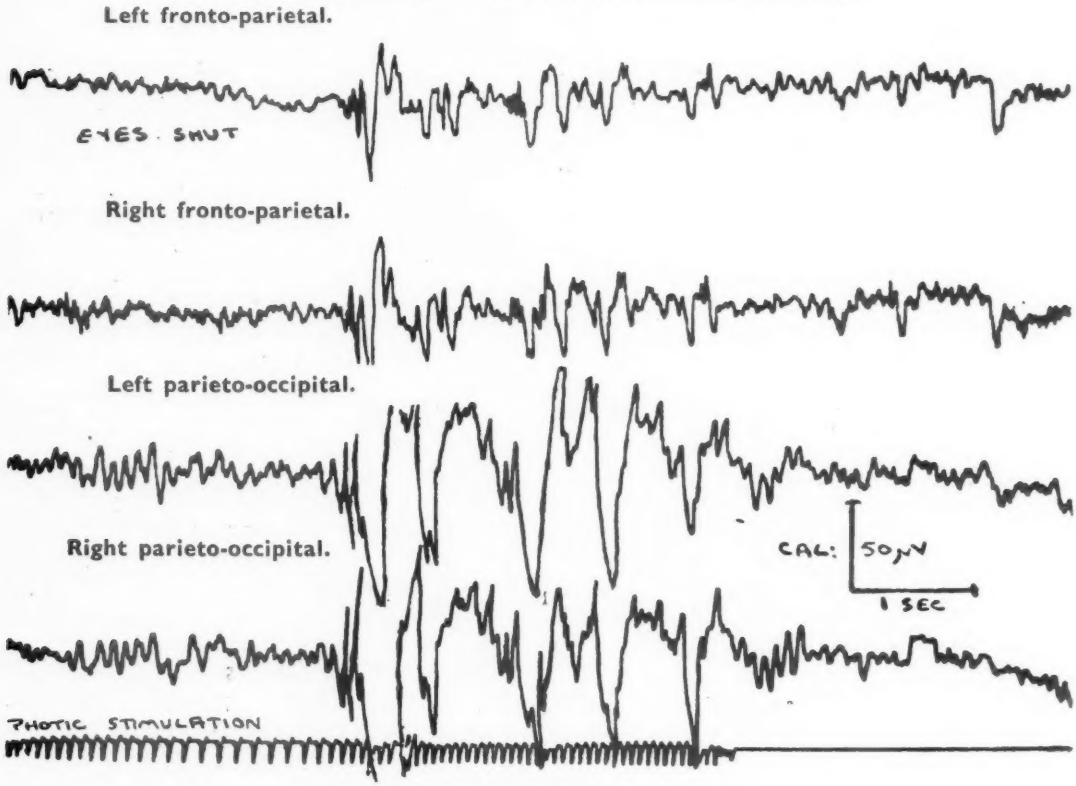


FIG. 4.—Evoked seizure patterns in a girl aged 9.

persisted throughout the record and the children were not unduly agitated or apprehensive. Fig. 5 shows a record from a girl aged 10 with dominant theta activity and absence of an alpha rhythm. There was one further record which was considered to be primarily organic with a well marked delta-and-spike focus in the left parietal lobe. Four children had further records taken; in two cases two repeats and in two a further single tracing. None of these differed significantly from the original. The table gives the results in detail for the various age groups.

ANALYSIS OF RECORDS

Record	5-6 yrs.	7-8 yrs.	9-10 yrs.	11-12 yrs.	13-16 yrs.	Over 16 yrs.	Total
Normal ..	9	6	5	–	1	5	26
Borderline normal ..	13	5	3	1	1	–	23
Epileptiform features ..	–	3	4	–	1	–	8
Epileptic ..	1	3	3	4	3	–	14
Immature features ..	5	7	8	4	2	2	28
Focal organic ..	–	–	–	1	–	–	1
Total ..	28	24	23	10	8	7	100

Discussion

Although there are numerous references to the E.E.G. in behaviour disorders there are few specific references to enuresis. Secunda and Finley (1942) examined a group of children with behaviour disorders including some with enuresis, and found a high proportion that they described as immature borderline or immature tracings. Michaels and Secunda (1944) investigated 122 cases in an attempt to evaluate the possible relationship between immature abnormal E.E.G.s and enuresis and other neurotic traits. They found a positive correlation between enuresis and an abnormal E.E.G. but this was not so in vague and complex behaviour disorders.

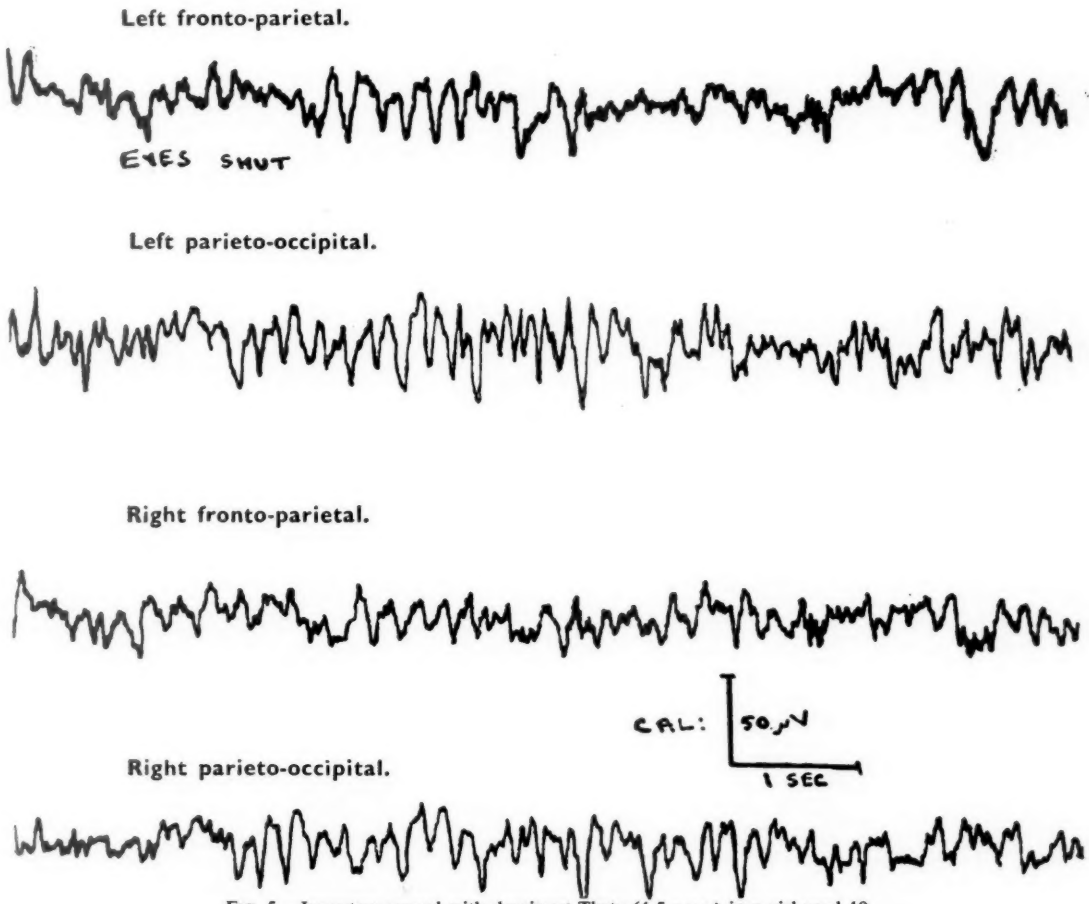


FIG. 5.—Immature record with dominant Theta (4-5 c.p.s.) in a girl aged 10.

Cattell and Pacella (1950), however, in contra-distinction, using a small sample of 42 patients of whom fewer than 45% were enuretic, found no difference in tracings taken from various types of behaviour disorder.

Gunnarson and Melin (1951) examined 96 enuretics after the third year of life. Sixty-four were continuously enuretic from birth, and 26 had had a dry period varying from a few months to several years. Only two showed an epileptiform E.E.G. which is a considerably smaller proportion than in our series. They found a greater proportion of abnormal records in the always wet children, with 52% having a slow record and 25% a moderately slow record, and they believed that this was to a great extent due to some form of brain change, most likely immaturity. Their results are comparable to our own.

Sessions Hodge and Hutchings (1952) examined electro-encephalographically 27 of a group of 131 enuretic children. Five of these showed a record of an epileptic nature while the other 22 showed a 'non-specific' abnormality varying in degree of severity.

Our results indicate that a high proportion of severe enuretics show an abnormal or borderline E.E.G. The principle abnormality is a 'too slow type of E.E.G.', as described by Gottlieb, Knott and Ashby (1945) in primary behaviour disorders. It is tempting to link up what might be called an 'immature' E.E.G. with an immature uninhibited cystometrogram, as described by Stalker and Band (1946), these being different aspects of basic failure of cortical development.

The number of epileptic records is rather surprising; it might have been that chance factors introduced an excess, despite the fact that many of the patients had spent a period of time in hospital where trained observation was possible.

It seems likely that a considerable proportion of severe enuretics who do not respond to any of the ordinary simple measures have in fact a physical basis for their disorder. The E.E.G. appears to be of value in determining the nature and severity of the basic disturbance.

Summary

The E.E.G.s from 100 cases of severe enuresis but without any organic condition were studied in detail.

Only 26 of these were completely normal and a further 23 were on the borderlines of normality.

Of the abnormal records 28 showed a too slow or immature type of record. A further one showed an organic type of tracing.

The remainder, 22 in all, were of an epileptiform type with 14 of these showing typical seizure patterns either at rest or during activation procedures.

We would like to thank all the clinicians who referred cases to us, including the staff of the Bristol Royal Hospital for Sick Children, and especially Dr. M. Boyd who investigated a considerable proportion of the cases. We should like to thank Miss Rockett and Miss Heaven, recordists, for their assistance, and Dr. R. E. Hemphill, Medical Superintendent, for permission to publish this paper.

References

Brill, N. Q. and Seidemann, H. (1941). *Amer. J. Psychiat.*, **98**, 250.
Cattell, J. P. and Pacella, B. L. (1950). *Ibid.*, **107**, 25.
Gibbs, F. A. and Gibbs, E. L. (1941). *Atlas of Electroencephalography.* Cambridge, Mass.
Gottlieb, J. S., Knott, J. R. and Ashby, M. C. (1945). *Arch. Neurol. Psychiat., Chicago*, **53**, 138.
Gunnarson, S. and Melin, K. A. (1951). *Acta. paediat. Uppsala*, **40**, 496.
Henry, C. E. (1944). *Electroencephalograms of normal children. Monogr. Soc. Res. Child. Dev.*, **9**, no. 3 (Serial No. 39).
Hewlett, M. G. T. (1951). *Electroenceph. clin. Neurophysiol.*, **3**, 513.
Hodge, R. Sessions and Hutchings, H. M. (1952). *Archives of Disease in Childhood*, **27**, 498.
Jasper, H. H. (1949). *Pediatrics*, **3**, 783.
Lindsley, D. B. (1939). *J. gen. Psychol.*, **55**, 197.
Michaels, J. J. and Secunda, L. (1944). *Amer. J. Psychiat.*, **101**, 407.
Pond, D. A. (1951). *Psychiatrie Sociale de l'enfant*, ed. Koupernik, C., pp. 275-283. Centre International de l'Enfance. Travaux et Documents II. Paris.
Secunda, L. and Finley, K. H. (1942). *New Engl. J. Med.*, **226**, 850.
Smith, J. R. (1938). *J. Gen. Psychol.*, **53**, 455.
Stalker, H. and Band, D. (1946). *J. ment. Sci.*, **92**, 324.
Turton, E. C. (1952). *Electroenceph. clin. Neurophysiol.*, **4**, 83.
Walter, V. J. and Walter, W. G. (1949). *Ibid.*, Suppl. 2, p. 63.
Walter, W. G. (1950). In 'Electro-encephalography', ed. by Hill, D. and Parr, G., pp. 206-207. London.

A CASE OF CONGENITAL HEMIHYPERTROPHY SHOWING VARIATIONS IN BONE AGE AND DEVELOPMENT

BY

F. STEPHEN CARTER and G. C. DOCKERAY

From King George VI Hospital, Nairobi, and the Medical Research Laboratory, Nairobi

(RECEIVED FOR PUBLICATION MARCH 13, 1953)

Although the ancient Greek and Roman sculptors recognized that the human frame was not symmetrical, it was not until 1822 that Meckel pointed out variations in size and shape of the two halves of the body, and the first clinical report of a patient with hemihypertrophy was made by Wagner in 1839. Since that day there have been only just over 100 cases reported throughout the world claiming total hemihypertrophy, and this is probably in excess of the truth if the name given to the condition is taken literally. Ward and Lerner (1947), in reviewing the case reports, state that necropsies had been recorded in only seven cases, and they added a case report of their own with necropsy findings, and concluded, according to their classification of hypertrophy, that their patient had congenital total hemihypertrophy. It is doubtful, however, if this claim can be accepted, as one set of paired organs, namely, the kidneys, was equal in size, and the two lobes of the thyroid were also apparently equal. In the absence of a necropsy, the diagnosis of congenital total hemihypertrophy has to be made on external appearances, with the assumption that the internal paired organs will also show hypertrophy on the affected side. That this assumption may be false is shown by the case quoted above, and also by the necropsy findings of the case recorded in this paper.

The chief interest in this case, however, lies in the radiological appearances of the wrists and hands, which show well marked differences in the extent of ossification of the carpal nuclei on the two sides, and also structural abnormality of the bones themselves.

Case Report

A male infant, said to be 18 months old, of the Munyore tribe, from the North Nyanza Province of Kenya, was referred from one of the City African child welfare clinics in Nairobi to King George VI Hospital on June 20, 1952, for investigation of his asymmetrical development and treatment for gastro-enteritis.

On examination, the face appeared symmetrical, but there was obvious enlargement of the left side of the body, apparently involving all the component parts. The skin of the left limbs was somewhat coarser than that of the right, and this impression was enhanced by an increase of subcutaneous tissue on the affected side. The muscle substance was increased on the left side, and this was most marked in the deltoid, triceps and biceps in the arms, and the gluteal group in the legs, although hypertrophy was evident throughout the smaller muscle groups in both the upper and lower limbs.

The infant suffered from frequent attacks of petit mal. There would be a sudden cessation of activity, his facial expression would become vacant, and his eyes take on a glassy appearance. This period of inactivity usually lasted only a few seconds, but on two occasions it was reported to have lasted for about a minute, causing considerable anxiety to the ward staff. On no occasion was an attack of grand mal, or Jacksonian epilepsy, witnessed.

After an initial response to therapy for the gastro-enteritis, there was a sudden relapse and death occurred within a few hours, despite resuscitative measures.

During the period of remission the infant's behaviour was considered to be somewhat retarded for his age, but he could not be considered an obviously mentally defective child. Despite the disproportion of his lower limbs, he was frequently to be seen standing up in his cot, and he appeared to be taking a reasonable interest in ward activities. There was, however, a certain dullness in his facial expression and a lack of alertness, but this could partly be attributed to the intercurrent infection. His powers of walking were not assessed, but there was a well marked compensatory scoliosis when he stood up in his cot.

Necropsy Findings. At necropsy, hypertrophy of the left side of the body, from the neck downwards, was confirmed. The difference in size of the various muscle groups was very obvious on dissection of the two sides. The long bones were excised and measured (Fig. 1 and Table 1). The only paired internal organs to show any noticeable difference in size were the kidneys, the left weighing 44 g. and the right 30 g. There was also a slight difference in weight of the two lungs, the left weighing 81 g., and the right 75 g., whereas the right lung is normally the

heavier of the two. In adults, the right lung varies from 480 to 680 g., and the left from 420 to 600 g. (Mallory, 1938).

The cerebral hemispheres, lobes of the thyroid, suprarenals and testes appeared equal on the two sides. The degree of dental eruption was the same on both sides, and there was no evidence of inequality of the two sides of the tongue.

TABLE 1

MEASUREMENTS OBTAINED FROM POST-MORTEM MATERIAL

	Right (cm.)	Left (cm.)
Mid-thigh circumference	17·7	24·0
Mid-calf circumference	14·0	17·4
Foot-print (length)	10·5	11·7
Humerus (length)	11·3	12·9
„ (circumference at narrowest point)	3·6	4·1
Radius (length)	10·3	11·4
Ulna (length)	9·5	10·3
2nd metacarpal (length)	2·9	3·1
Femur (length)	13·7	14·8
„ (circumference at narrowest point)	3·5	3·9
Tibia (length)	12·1	13·1
Fibula (length)	10·5	11·5

* Bone measurements include epiphyseal cartilages.

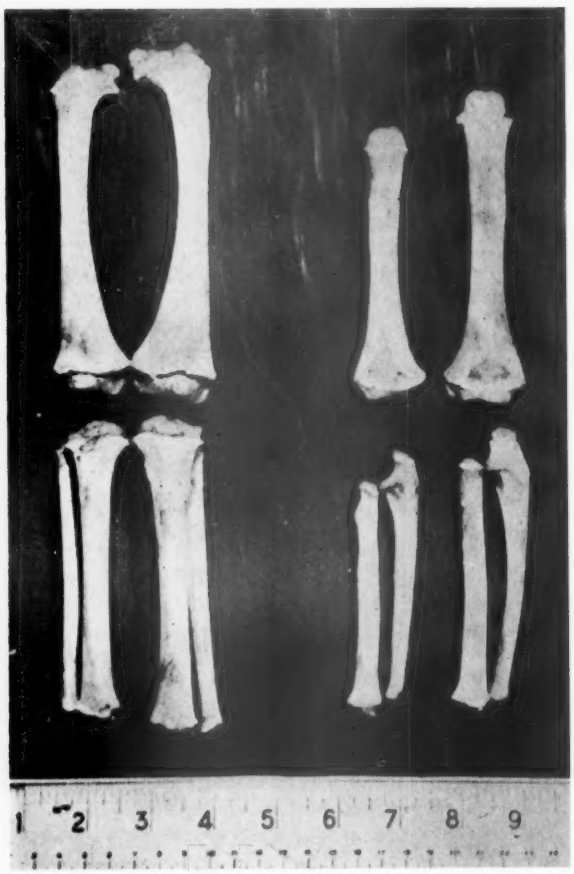


FIG. 1.—Photograph of the long bones, excised at necropsy, showing hypertrophy of those on the left side of the body.

Radiological Findings. Radiographic examination of the skull showed no abnormality, and the sella turcica was well within normal limits. Dental development was equal on both sides. The radiological appearance of the long bones and pelvis showed considerable hypertrophy on the affected side, and the wrists showed evidence of variation in bone age (Figs. 2 and 3).

Dr. W. G. S. Hopkirk kindly examined the radiographs of the wrists, and gives the following report on the bone age, based on the studies of Mackay (1952) for African children:

FIG. 2.—Radiograph of both wrists. Left wrist shows well developed centres of ossification for the capitate, hamate, triquetrum, and inferior radial epiphysis. Right wrist shows only the capitate and hamate, although a minute centre of ossification for the triquetrum is visible on the original radiograph.

Right Wrist	Left Wrist
Carpus (if tiny triquetral centre is disregarded) 18 months	3 years 6 months
Inferior radial epiphysis, still absent. Less than 18 months	Present 18 months
Metacarpal diaphyses, 18 months	2 years 6 months

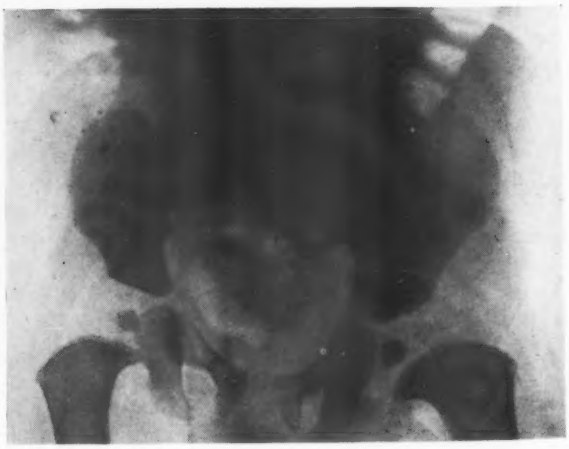


FIG. 3.—Radiograph of the pelvis, showing considerable enlargement of the left ilium, and increased depth of the soft tissues on the left side.

Dr. Hopkirk also reports that '. . . the structure of the metacarpals, and to a lesser extent of the radius and ulna, is not normal. There is less individual shaping than would be expected from the known age, and the appearances suggest that there has been slight cortical atrophy from within and a lack of normal trabecular formation. This suggests some hypertrophy of the bone marrow, though not to the extent often seen in severe haemolytic anaemias . . . Epiphyseal development is retarded very considerably . . . Having regard to the absence of the metacarpal and phalangeal epiphyses the bone age on both sides should be about 1 year.'

Discussion

There has been much speculation as to the aetiology of congenital hemihypertrophy, and the various theories were reviewed by Schwartzman, Grossman and Dragutsky (1942). Endocrine imbalance, congenital syphilis, vascular lesions, lesions of the brain, and embryonic defects of the vegetative nervous system, have all had their advocates, but the theory propounded by Gesell (1927), is the one to which most credence is given among the more recent authors. Gesell considered that the condition was due to an atypical form of twinning occurring in the very earliest divisions of the fertilized ovum. Asymmetry was described in a 10 mm. human embryo by Phisalix in 1888.

Campbell (1923) described a case of hypertrophy due to neurofibromatosis, and cases have been recorded by McFarland (1928) and Williams (1951) where the condition was due to abnormalities of the lymphatic system, although the latter case also showed hypertrophy of the bones of the right forearm and hand.

The frequency with which other congenital abnormalities coexist with congenital hemihypertrophy has been put as high as 50% by Ward and Lerner (1947). The commonest lesions are cutaneous naevi and telangiectases, mental deficiency being the next most frequent. Gesell (1927) collected 53 cases of congenital hemihypertrophy, and eight of these were mentally defective. Lenstrup (1927) published a series of eight cases, one of which was mentally defective, and another suffered from convulsions. Other authors have recorded cases of mental deficiency, and the frequency with which it occurs has been estimated at 15 to 20% (Wakefield and Hines, 1933; Schwartzman *et al.*, 1942). Other congenital abnormalities that have been described include congenital heart disease, hypospadias, cryptorchidism, supernumerary nipple, polydactylism, synostosis, and total absence of the thyroid. The affected side of the body may also show thickening of the hair, premature eruption of the teeth, abnormal growth of the nails and excessive sweating.

In the case recorded here no anatomical congenital abnormalities were discovered, but the degree of intelligence was considered to be low, and the infant also suffered from numerous attacks of petit mal.

Heredity appears to have no influence in the great majority of cases (Worster-Drought, 1951), but a high proportion of siblings may show other congenital abnormalities (Halperin, 1931). Hemihypertrophy has, however, been described in a mother and daughter (Scott, 1935), and also in a brother and sister (Reed, 1925).

The literature on the subject of hemihypertrophy contains a number of references to radiological enlargement of the bones on the affected side. In the series of eight cases described by Lenstrup (1927), three of them showed radiological enlargement of the bones, but an increase in bone age on the affected side appears to occur infrequently, as only two such cases have been found recorded (Scott, 1935; Williams, 1951). Gesell (1927), however, included in his case report of a girl of 2 years old a reproduction of a radiograph showing the centre of ossification for the semilunar bone on the affected side, which was absent on the normal side. This fact is recorded in a table of measurements, but no comment is made in the script. It is probable that advancement of bone age occurs more frequently than is recorded as many cases had reached bone maturity before being investigated. Worster-Drought (1952) comments that . . . 'enlargement, whether hemihypertrophy or merely hypertrophy of one limb, can include advanced bone age, that is as compared with the opposite and normal side, while other cases show merely enlargement without apparent advance in bone age' . . .

Dr. J. F. Brailsford, who has also studied the radiographs in this case, states:

> 'The bones of the hands do not show normal architecture. They have not the exquisite shape of the normal; the cortical compact tissue is reduced to linear proportions; the cancellous structure is of a coarser mesh, which is defective. These features suggest an established disturbance in ossification such as we see in congenital anaemias.
>
> 'The right hand shows a stage of ossification of the carpus which is in agreement with the normal, but lack of ossification in the epiphyses of the metacarpals and the radius suggests delay.
>
> 'The hypertrophied left hand shows bones which are all some degree larger than the right; the ossification of the carpals is in advance of the normal but this is not supported by the lack of ossification in the epiphyses of the metacarpals and phalanges.
>
> 'The case clearly indicates that the times for ossification of the epiphyses and the carpal nuclei are variable, and considerable latitude must be allowed in estimating bone age from either. So many factors influence early ossification but do not neces-

> sarily influence the carpal nuclei to the same degree as the metacarpal and phalangeal epiphyseal nuclei. Inflammatory processes can cause delay in ossification yet it would seem that an increased blood supply to a limb appears to advance the ossification beyond that of the opposite limb, but here we see evidence of advance of the carpal but delay in the metacarpal and phalangeal—a clear indication that our knowledge of growth is very defective . . .'

Another feature of interest found at necropsy concerned the size of the various 'paired' internal organs. Although there was radiological evidence of skeletal hypertrophy of ribs and pelvis as well as both upper and lower limbs on the left side, yet the testes and suprarenals were of the same size on both sides of the body. Ward and Lerner (1947) had a similar experience when, at the necropsy of a patient who had apparently congenital total hemihypertrophy, they found the kidneys to be equal in size, and the lobes of the thyroid also appeared identical.

If the theory is accepted that hemihypertrophy is due to an abnormal form of twinning at a very early stage after fertilization of the ovum, it would seem reasonable to expect the hypertrophy to involve all the structures within the embryological segments so affected. It is apparent that this is not always so, and therefore it is obviously unwise to assume congenital total hemihypertrophy on external appearances alone, as this is the second case out of a total of nine necropsies recorded in the literature where equality of such paired organs has been found.

Summary

A case of left-sided congenital hemihypertrophy with necropsy findings is reported.

Radiologically, the carpal bones showed apparent advancement of bone age on the affected side, but also retardation in development of the epiphyses of the metacarpals and phalanges on the same side, combined with an abnormal structure of the bones themselves.

As certain internal paired organs within the embryological segments affected by the hypertrophy were found to be equal in size at necropsy, namely, testes and suprarenal glands, it is considered unwise to assume a diagnosis of congenital total hemihypertrophy on external appearances alone.

We are indebted to the Hon. Director of Medical Services, Kenya, for permission to publish this paper. We also wish to express our thanks to Dr. W. G. S. Hopkirk and Dr. J. F. Brailsford for their assistance and interpretation of the radiographs, and to Dr. J. A. T. Henry, who referred the child to us in the first instance.

References

Campbell, W. C. (1923). *Surg. Gynec. Obstet.*, **36**, 699.
Gesell, Arnold (1927). *Amer. J. med. Sci.*, **173**, 542.
Halperin, G. (1931). *Arch. intern. Med.*, **48**, 676.
Lenstrup, E. (1927). *Acta paediat., Uppsala*, **6**, 205.
Mackay, D. H. (1952). *Trans. roy. Soc. trop. Med. Hyg.*, **46**, 135.
Mallory, F. B. (1938). *Pathological Technique*, p. 375. Philadelphia.
McFarland, B. L. (1928). *Brit. med. J.*, **1**, 345.
Meckel, J. F. (1822). Quoted by Halperin (1931).
Phisalix, C. (1888). *Arch. Zool. exp. gén.*, ser. 2, **6**, 279. Quoted by Wakefield and Hines (1933).
Reed, E. A. (1925). *Arch. Neurol. Psychiat., Chicago*, **14**, 824.
Schwartzman, J., Grossman, L. and Dragutsky, D. (1942). *Arch. Pediat.*, **59**, 637.
Scott, A. J. (1935). *J. Pediat.*, **6**, 650.
Wagner, H. (1839.) Quoted by Schwartzman *et al.* (1942).
Wakefield, E. G. and Hines, E. A. (1933). *Amer. J. med. Sci.*, **185**, 493.
Ward, J. and Lerner, H. H. (1947). *J. Pediat.*, **31**, 403.
Williams, J. Aled (1951). *Archives of Disease in Childhood*, **26**, 158.
Worster-Drought, C. (1951). *The British Encyclopaedia of Medical Practice*, 2nd ed., vol. 6, p. 464. London.
—— (1952). Personal communication.

ENTEROGENOUS CYST OF THE MEDIASTINUM

BY

T. A. SALE

From the Royal Liverpool Children's Hospital

(RECEIVED FOR PUBLICATION APRIL 27, 1953)

Enterogenous cyst of the mediastinum is not a common condition. According to Bickford (1949) 40 cases have been reported. Of these, 24 were lined by purely gastric mucosa (this includes the case reported by him), four had purely intestinal epithelium and 12 were composite.

This paper is presented as a further instance of an enterogenous cyst which was removed successfully at thoracotomy.

Case History

The patient was a baby girl born of a healthy mother who had had a normal pregnancy. The baby was admitted when aged 3 months, on March 1, 1950, because of bronchitis, which had been present for one week.

Examination revealed cyanosis and distressed respirations, with diminished expansion of the chest over the right base, and a diminished percussion note. A diagnosis of bronchopneumonia was made. Mantoux tests were negative. Radiographs (Figs. 1 and 2) showed a large oval tumour lying posteriorly in the upper two-thirds of the right side of the chest. From time to time some stridor was noted. Her weight gain was not satisfactory. Mr. F. Ronald Edwards advised thoracotomy for a possible gastrogenic cyst of the mediastinum or possibly ganglioneuroma.

On May 24, 1950, the chest was opened through the bed of the right sixth rib. In the posterior mediastinum was a tensely cystic swelling 4 cm. × 2 cm. × 1·5 cm. A few millilitres of clear fluid was aspirated. This later was analysed as clear mucoid fluid with no trypsin, pepsin or free hydrochloric acid. The chloride content was 700 mg. %. The cyst was excised and the chest closed without drainage. There was a small extra posterior upper lobe segment. On June 3, 1950, the baby became dyspnoeic and cyanosed. She had signs of an effusion on the right side of the chest and 160 ml. of milky alkaline fluid was aspirated. This fluid did not recur and she was discharged on June 30, 1950. Since that time she has continued to gain weight and the chest has remained clear.

Section of the cyst showed a thick muscular wall (Figs. 3 and 4) of smooth muscle divisible into two layers running at right angles to each other. There was a thin muscularis mucosae on which there was a thin zone of coiled tubular epithelium. Finally there was a layer of tall columnar epithelium. Oxyntic cells were absent. The mucosa was enterogenous but not typically gastric.

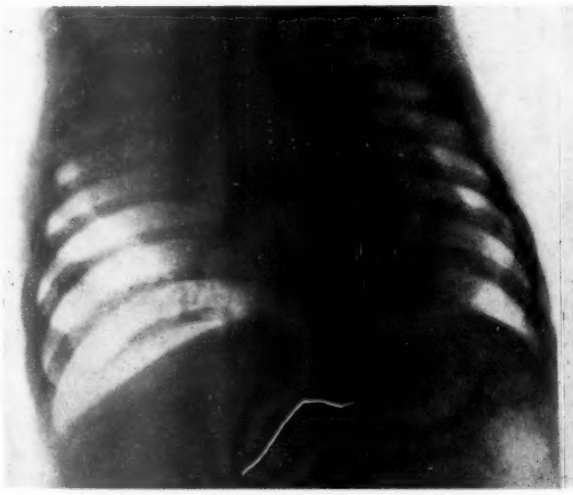


FIG. 1.—Rounded tumour on the right side of the chest.

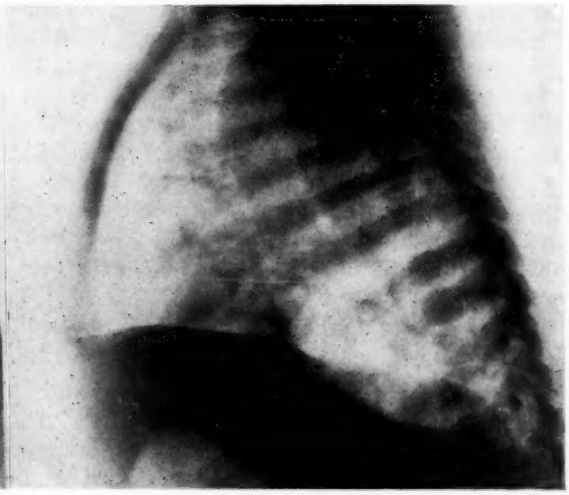


FIG. 2.—Lateral film showing the rounded tumour in the posterior mediastinum.

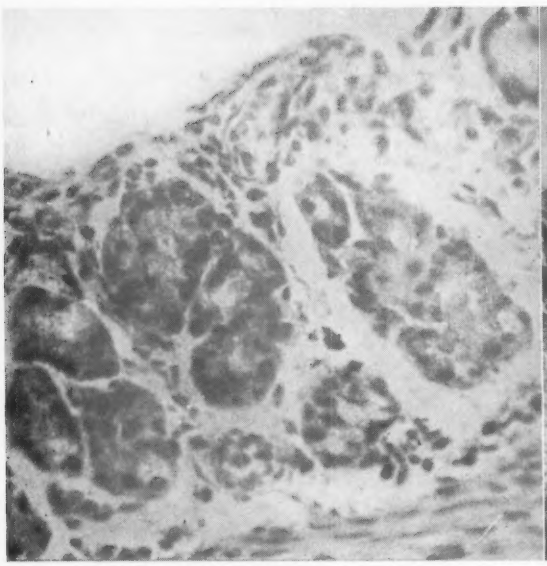


FIG. 3.—High-power photomicrograph of section showing the intestinal mucosal lining of the cyst. ×400.

FIG. 4.—Low-power photomicrograph of section showing the arrangement of the muscle layers and mucosa. ×88.

The fluid removed from the chest contained large numbers of lymphocytes and many fat globules.

Incidence

These cysts may be found on either side of the chest, but a little more commonly on the right (1·5 to 1) (Olenik and Tandatnick, 1946).

Males are affected a little more often than females (1·5 to 1) (Olenik and Tandatnick). It is predominantly a condition of young children. Eighteen cases occurred under 4 years of age (Steele and Schmitz, 1945). A case has been described in which the patient was a 15-year-old girl (Steele and Schmitz), another a 10-year-old girl (Dickson, Clagett and McDonald, 1946) and the oldest appears to be that of a 54-year-old man (Adams and Thornton, 1943). The cysts are invariably confined to the chest. One extended below the diaphragm (Dickson *et al.*) and three thoracic cysts described by Gross, Neuhauser and Longino (1951) were found to be intestinal diverticula arising in the abdomen. Truly thoracic cysts may, however, be associated with intra-abdominal cysts (Poncher and Milles, 1933).

Pathology

The cysts vary in size, shape and position in the chest. They may be as small as 2 × 3 × 2 cm. (Ward and Krahl, 1942) or as large as 14 × 20 × 5 cm. (Black and Benjamin, 1936). They are usually unilocular but may be multilocular (Ward and Krahl). The wall consists of two muscle layers placed at right angles to each other. There is a muscularis mucosae. The lining may be of gastric, intestinal or bronchial epithelium, singly or all found in the one specimen. The lining membrane may be atrophied and thus unidentifiable. When gastric mucosa is present there may be peptic ulceration with haemorrhage into the cyst or perforation of its wall. The blood supply of the cyst is derived from local vessels. Specially stained sections of the wall show the presence of ganglion cells (Böss, 1937; Seydl, 1935). The contents may be viscid, opalescent, milky or haemorrhagic. Davidson and Brown (1947) analysed the fluid from a cyst; the cholesterol content was 10 mg. %, protein 1·6 g. %, *p*H 7·8, and there was no free hydrochloric acid or pepsin.

Ladd and Scott (1944) analysed one specimen and showed that the cyst contained 360 ml. fluid. The reaction was acid, the specific gravity was 1010, chlorides 114 mg. %, bicarbonate 34 volumes %, and cells 560 per ml. (80% polymorphs). In a second case they withdrew 10 ml. of thick, viscid fluid containing 700 cells per ml.

Symptomatology

It must be realized that there may be no symptoms at all, and the condition is found on routine radiology (Steele and Schmitz). The symptoms may be due to the swelling itself, to local pressure effects, to complications within the cyst or to all three. There may be general systemic disturbances.

Symptoms Due to the Swelling. These are not common but Ward and Krahl in a report on a child aged 9 weeks remark that the mother noticed a

progressive enlargement of the right side of the chest.

Symptoms Due to Pressure Effects. The main structure affected in this way is the trachea. Stridor, respiratory wheezing and a brassy cough may be present. Cyanosis and dyspnoea and signs of bronchitis, bronchopneumonia, atelectasis and bronchiectasis may be present as secondary manifestations of the presence of the cyst. Erosion of the vertebral bodies and ribs may occur (Steele and Schmitz, 1945; Ladd and Scott, 1944).

Symptoms Due to Complications in the Cyst. These are due to the occurrence of peptic ulceration and its associated sequelae. Perforation into adjacent structures gives rise to well marked symptoms and signs. Thus haemoptysis, pneumothorax or empyema may develop.

General Symptoms. There may be failure to thrive, feeding difficulties, unexplained anaemia, and some babies have attacks of screaming and drawing up of the legs.

Investigation

Radiological examination of the chest is the most satisfactory way of establishing the diagnosis. There is a rounded swelling in the chest. There may be tracheal or bronchial compression from behind forwards (Lindquist and Wulff, 1947) and radiological signs of lung compression with or without infective changes. Wyllie and Pilcher (1943) have stated that the radiological signs are those of (*a*) a space-occupying lesion, (*b*) some degree of collapse of the lung, (*c*) obstructive emphysema, and (*d*) a picture suggestive of a pleural effusion, with, however, a clear costophrenic angle or a rounded contour of the angle. They also stress that good lateral films are essential to show the position of the cyst in the posterior mediastinum. The details of the cyst shadow may be obscured by secondary changes in the lungs or by pleural fluid (Ladd and Scott, 1944). Rarely, erosion of the ribs and vertebral bodies may be seen (Mixter and Clifford, 1929; Ladd and Scott).

Cassel, Cunningham and Weisel (1950) report in a man aged 24 a subcarinal widening with elevation of the right main bronchus on bronchoscopy. When the cyst is large bronchoscopy is of little value, but when small the clinical picture may resemble that associated with an inhaled foreign body or tuberculous tracheo-bronchial glands, and here bronchoscopy is essential (Wyllie and Pilcher). They also stress that tuberculosis must be excluded.

Paracentesis of the cyst has been performed. Ward and Krahl withdrew 15 ml. of thick fluid resembling old blood. Wyllie and Pilcher aspirated 10 ml. of blood-stained fluid which had a deposit of serosal cells and some 'fat' phagocytes. This mode of examination is deprecated by Lindquist and Wulff. They maintain that the nature of all mediastinal cysts should be proved by thoracotomy. Wulff operated on a child with a so-called cyst and found a large cavernous haemangioma. The cyst may, however, be aspirated if it is causing acute suffocation (Lindquist and Wulff).

Treatment

The general opinion prevailing is that thoracotomy should be performed and the cyst excised (Cassel *et al.*, 1950; Adams and Thornton, 1943; Bickford, 1949).

Ladd and Scott maintain that extirpation may be difficult because of adhesions, especially where there has been peptic erosion in the cyst. They advise marsupialization of the cyst and destruction of the lining membrane. They showed in one case that the cyst and the oesophagus had a common wall. In the operation reported here the dissection was performed under clear vision without any undue difficulty.

Theories of Causation

The aetiology of the condition has aroused much speculation. Although six possibilities have been put forward by Cassel *et al.*, three main theories should be considered.

One is that the cyst is due to a persistent foetal diverticulum. This is based on the work of Lewis and Thyng (1908), who have demonstrated these cysts in the pig, rabbit and human embryos. Ladd and Scott point out that diverticula resembling those described by Lewis and Thyng are rare in early post-natal life and also that they are most common in the region of the duodenum, whereas alimentary duplications are most common in the lower jejunum and liver.

The second theory postulates that the cysts are derived from omphalo-mesenteric remnants. This is based on the writing of Fitz (1884). The theory does not explain the occurrence of alimentary cysts down the gastro-intestinal tract towards the rectum and has difficulty in explaining how these cysts in the abdomen derive their blood supply.

The other theory is based on Keith's (1948) assertion that alimentary atresia and duplication are analogous. He proposes that this condition is due to an error in vacuolization in which there is a failure of coalescence of the vacuoles in the transverse diameter.

Summary

A case is reported of a 3-month-old baby in whom a cyst, lined by intestinal mucosa, was removed

from the mediastinum by operation. Convalescence was complicated by a chylothorax which was cured by a simple aspiration. The features and the literature of mediastinal gastro-enterogenous cysts are reviewed.

I wish to express my thanks to Dr. H. G. Farquhar, under whose care the baby was admitted and investigated, to Mr. F. Ronald Edwards, to Dr. R. E. Rewell for the pathological report and microphotographs and Miss Norah Walker for the x-ray prints.

BIBLIOGRAPHY

Adams, W. E. and Thornton, T. F. (1943). *J. thorac. Surg.*, **12**, 503.
Bickford, B. J. (1949). *Brit. J. Surg.*, **36**, 410.
Black, R. A. and Benjamin, E. L. (1936). *Amer. J. Dis. Child.*, **51**, 1126.
Böss, C. (1937). *Virchows Arch. path. Anat.*, **300**, 166.
Carlson, H. A. (1943). *J. thorac. Surg.*, **12**, 376.
Cassel, M. A., Cunningham, R. T. and Weisel, W. (1950). *Ibid.*, **19**, 138.
Davidson, L. R., and Brown, L. (1947). *Ibid.*, **16**, 458.
Davis, E. W., and Salkin, D. (1947). *J. Amer. med. Ass.*, **135**, 218.
Dickson, J. A., Clagett, O. T. and McDonald, J. R. (1946). *J. thorac. Surg.*, **15**, 318.
Fitz, R. H. (1884). *Amer. J. med. Sci.*, **88**, 30.
Gross, R. E., Neuhauser, E. B. D. and Longino, L. A. (1950). *Ann. Surg.*, **131**, 363.
——, Holcomb, G. W. Jr. and Farber, S. (1952). *Pediatrics*, 9, 449.
Keith, A. (1948). *Human Embryology and Morphology*, 6th ed. London.
Ladd, W. E. and Scott, H. W. (1944). *Surgery*, **16**, 815.
Lewis, F. T. and Thyng, F. W. (1908). *Amer. J. Anat.*, **7**, 505.
Lindquist, N. and Wulff, H. B. (1947). *J. thorac. Surg.*, **16**, 468.
Matheson, A., Cruickshank, G. and Matheson, W. J. (1952). *Archives of Disease in Childhood*, **27**, 533.
Mixter, C. G. and Clifford, S. H. (1929). *Ann. Surg.*, **90**, 714.
Nicholls, M. F. (1940). *Brit. J. Surg.*, **28**, 137.
Olenik, J. L. and Tandatnick, J. W. (1946). *Amer. J. Dis. Child.*, **71**, 466.
Poncher, H. G. and Milles, G. (1933). *Ibid.*, **45**, 1064.
Schwarz, H. and Williams, C. S. (1942). *J. thorac. Surg.*, **12**, 117.
Seydl, G. N. (1935). *Frankfurt, Z. Path.*, **52**, 346.
Steele, J. D. and Schmitz, J. (1945). *J. thorac. Surg.*, **14**, 403.
Valle, A. R. and White, M. L. (1946). *Ann. Surg.*, **123**, 377.
Ward, I. M. and Krahl, J. B. (1942). *Amer. J. Dis. Child.*, **63**, 924.
Wyllie, W. G. and Pilcher, R. S. (1943). *Archives of Disease in Childhood*, **18**, 34.

THE TREATMENT OF ASCARIS INFECTION WITH VELARDON

BY

J. H. P. JONXIS and H. BEKIUS

From the Children's Clinic, the University Hospital, Groningen, the Netherlands

(RECEIVED FOR PUBLICATION MARCH 18, 1953)

Ascaris infection is still very common, mainly in children and especially in unhygienic conditions. In the human intestinal tract only that species of ascaris parasitic in man can develop. Every ascaris infection is caused by larvae from eggs which have been deposited in the soil with human faeces, and the ascaris egg must have developed for some time in the soil before it is capable of infecting another host. Direct infection by newly evacuated faeces is not possible. The absence of good water-closets and sewerage greatly increases the risk of infection, as also does the manuring of gardens with human faeces. It is obvious that under these conditions eating raw vegetables will almost certainly cause infection. Another source of infection is found in playgrounds for toddlers.

The complaints caused by ascaris vary and in many cases are vague. Not only do such symptoms as poor appetite, abdominal pain (often around the navel) and diarrhoea occur, caused by parasites in the intestinal tract, but also those connected with the passage of the larvae from the intestine through the liver to the lung and trachea causing as they pass bronchitis and transient lung infiltration. Eosinophilia, so often associated with ascaris infection, is suggestive of hypersensitivity. Other signs of allergy may be meningism, sterile meningitis, urticaria and pains in the joints. As long as the condition in the gastro-intestinal tract is normal, the worms give little trouble locally. However, as soon as the acidity of the duodenal content changes or there is a rise in temperature, the worms tend to migrate, causing various complications.

In combating ascaris, it is essential to prevent new infections. Good sewerage is one of the first conditions. In infected areas it is necessary to free as many ascaris carriers as possible of worms, not only as treatment but also to get rid of sources of infection. It should be borne in mind that in many cases a single course of treatment is not sufficient, even if all worms are expelled. In many cases the patient is also infested with larvae which are unaffected by treatment. In three or four weeks these have developed into new worms and the faeces will again contain eggs. It is often necessary, therefore, even if renewed infection is ruled out, to repeat the course of treatment with an interval of some weeks.

Oil of chenopodium in the correct dosage is the most potent anthelmintic. However, it is so toxic that it cannot be administered several times at short intervals to the same patient. Moreover, owing to its toxicity it is hardly suitable for mass treatment of entire infected groups of the population, a procedure which is highly desirable in the fight against ascaris. Santonin is less toxic but also far less effective, while a high dosage may cause reactions in the central nervous system. One of the first symptoms is a disturbance in colour vision. Hexylresorcinol is very active. It is far less toxic than oil of chenopodium and santonin. However, it is less suitable for children, since it has to be taken in capsules. The preparation itself causes damage to the mucosa of the mouth and oesophagus.

In spite of the use of anthelmintics and increased hygienic precautions, ascaris infection in man has been little reduced. The infection can be effectively combated only if an anthelmintic is available which is innocuous to the host of the parasite, so that administration may be repeated without causing untoward effects.

In some tropical regions papain was used as an anthelmintic as early as the seventeenth century, but so far apparently it has not been generally applied. Papain is the dried latex from the unripe fruit of *Carica papaya*. It contains an enzyme of the same name with a strongly proteolytic action, and in view of this property it is used for the production of protein hydrolysates. It affects the cuticula of the worm, causing the parasite to fall a victim to the intestinal juices. The shell of the eggs is also affected, so that they are rendered harmless. Since papain is innocuous to man, it is an almost perfect anthel-

mintic, provided the concentration in the intestine is kept sufficiently high for some time.

In the children's clinic of the University Hospital at Groningen we have tested an anthelmintic of which the effect is based on the activity of papain.

Velardon (N. V. Organon, Oss.) is available in packages of 20 g. granules containing 10 g. of papain activated with 0·5 g. of cysteine. The papain is standardized according to the method of Balls and Hoover (1937). The effect of papain on living ascarides is verified as follows. Papain suspensions are prepared in concentrations of 0·25%, 0·5%, 1% and 2%, and 50 ml. of each suspension is brought into contact with perhaps two living ascarides. The ascarides are first killed by the ferment, then disintegrated and finally dissolved.

The following table gives the results of this test:

Batch	Concentration (%)	30 Min.	75 Min.	2 Hours	3 Hours	4 Hours
811/51	2	Alive	+	Some corrosion	Corrosion continues	Dissolved
Res. P. 236	1	Alive	Alive	+	Corrosion	Dissolved
	0·5	Alive	Alive	Alive	+	Corrosion
	0·25	Alive	Alive	Alive	+	No corrosion yet

As there is a high incidence of ascariasis in the northern provinces of the Netherlands, there was sufficient material for research. Treatment was given to those children who passed many ascarides in the faeces, most of whose histories suggested ascariasis. Several children had evacuated worms spontaneously. Others had a poor appetite and showed disturbances in absorption, and some abnormalities of the lungs for which no cause other than ascaris could be found. These complaints disappeared after treatment.

The result of treatment with 'velardon' was judged by the presence of ascaris eggs in the faeces in the first weeks after treatment, and if there was any doubt about the result, it was followed by a course of oil of chenopodium.

In order to reduce the contents of the intestine as far as possible at the beginning of treatment, an infusion of senna was given on the previous day, and during treatment the food intake was drastically reduced. The anthelmintic, consisting of 20 g. granules containing an activated papain preparation, was administered to the fasting patient on the following morning. Children who are not able to take the full 20 g. straight off can do so in small portions in the course of an hour. In the next four or five hours practically no food was given. Administration of the anthelmintic was not followed by a laxative. This is not necessary as the papain preparation is not toxic and the laxative would lower the concentration of the papain and consequently reduce its activity. Moreover, the time during which the worm is in contact with the enzyme would be reduced. As a result of not administering a laxative, no dead worms will be found in the faeces in the majority of cases. They disintegrate in the intestinal canal. This applies partly also to worm eggs, damaged specimens of which may be found in the faeces.

Originally we gave a laxative after treatment. This caused evacuation of dead worms but the number of cases in which ascaris eggs continued to be found in the faeces was still fairly high. After a change in the method of treatment a marked improvement was observed.

Reappearance of eggs in the faeces five or six weeks after treatment does not imply that worms were left in the intestine but is probably due to worms having developed from larvae which at the time of treatment were infesting the liver or spleen.

Altogether 20 children were treated, all under 8 years of age. All had numerous ascaris eggs in the faeces. Nine had spontaneously evacuated worms. Practically all had vague abdominal complaints which might have been due to ascaris infection. In six cases the complaints were so marked that the children were admitted to the clinic for ascariasis. In 15 cases the results were such that no more ascaris eggs were found in the faeces after a single course of treatment.

A course of treatment with oil of chenopodium with which we followed up this therapy to make quite certain of a cure, did not produce any more ascarides either, except in five cases. These were children in whom heavy infestation was suspected. In order to get an impression of the number of worms which had remained behind, they also were given a course of treatment with oil of chenopodium for three days three times as many drops as the number of years of the child's age.

The number of ascarides expelled was:

In the first patient	..	50
In the second patient	..	6
In the third patient	..	21
In the fourth patient	..	45
In the fifth patient	..	56

In Cases 3 and 5 eggs were still found in the faeces after this therapy. In Case 3 renewed 'velardon'

therapy caused them to disappear. In Case 5 the second course of treatment with 'velardon' had to be followed by renewed therapy with oil of chenopodium, after which another 20 worms were evacuated. Tests on the faeces were still positive and a third course of 'velardon' treatment was needed.

These results show that it is possible in many cases to cure moderately infected children by a single course of treatment with this preparation. If the number of worms is very large the intestine is so filled with them that the concentration of the anthelmintic is too low to produce a conclusive result. The same applies to oil of chenopodium. In such cases repeated treatment is required. In view of its low toxicity, 'velardon' is very suitable for repeated therapy.

It is a remarkable fact that 'velardon' therapy of ascaris infection rarely causes evacuation of ascarides. The worms disintegrate entirely in the intestine. This does not, however, give rise to absorption of large quantities of toxic products. None of the children showed any reaction during treatment. Activated papain is, therefore, an excellent therapeutic agent against ascaris. It is not toxic and does not produce side-effects. Repeated treatment is required only in heavy infestations. However, the same applies to other anthelmintics.

In this investigation we have tried to form an opinion on 'velardon' as an anthelmintic in ascariasis only. Little attention was paid to its effect on other intestinal parasites, but we have the impression that good results might also be obtained in oxyuris infection.

REFERENCE

Balls, A. R. and Hoover, S. R. (1937). *J. biol. Chem.*, **121**, 737.

A HISTORY OF INFANT FEEDING

PART III: EIGHTEENTH AND NINETEENTH CENTURY WRITERS

BY

IAN G. WICKES

(RECEIVED FOR PUBLICATION JULY 2, 1953)

Eighteenth Century Writers

The social conditions in the eighteenth century have been described at some length in Part II because it is impossible to study the progress of infant feeding without examining the background which has so profoundly influenced its every aspect. We shall now proceed to consider in more detail the individual contributions to the subject which were made by the more important physicians who lived and worked in this momentous epoch.

M. Ettmüller (1644-83) strictly belongs to the seventeenth century but his 'Practice of Physic' (p. 677), which he wrote when he was professor at Leipzig, was first translated into English in 1699, and the second edition, from which the following excerpts are taken, was published in 1703 under the title of 'Ettmüller Abridged'. The diseases of men and women are fully dealt with in the earlier part and the diseases of children occupy Book V.

This work, though scarcely original in most respects, contains the first definite instruction to put the baby to the breast during the colostrum period, a practice which folk-lore usually forbids. Ettmüller also believed that it was unnecessary to give honey or castor oil to rid the newborn infant of the highly poisonous meconium which 'taints the Nourishment with a preternatural Acidity', for the 'beestings' were purgative. He believed also that breast milk could not be assessed so much by its thickness or taste, but rather by a variation in its more subtle qualities as exemplarized by the transmission of the nurse's character and temperament. The usual caution against overfeeding is found on page 621: 'Nothing is more apt to disorder the child than suckling it too often, since large quantities of Milk stagnating in the Stomach, must needs corrupt and occasion Crudities, especially if fresh Milk be pour'd in before the preceeding be digested.' On the next page he traces a curious sequence starting with the evil effects of venery on the milk of the nurse which causes it to curdle in the infant's stomach setting up in him an antipathy for cheese in later life—a train of events which heralds the case histories of modern psychiatrists!

Finally Ettmüller comments upon the practice of pre-chewing the food by the nurses (p. 623):

> 'Tis customary among Nurses to attenuate the Child's food in their Mouths before they give it, and indeed 'tis true that a healthy Nurse's Spittle is of use for promoting a quick digestion: But if scorbutic Salts be lodged in her gums, or if a Cacophymy prevail in her Body, it is too apt a Vehicle for conveying a morbifical Tincture into the Child's Body.'

William Cadogan's (1711-97) 'Essay upon the Nursing and Management of Children from their Birth to 3 Years of Age' was written for, and subsequently published by, the General Committee of

FIG. 6.—William Cadogan, a pioneer in infant feeding. Reproduced from 'History of Paediatrics' by Still by kind permission of the Oxford University Press.

the Foundling Hospital in 1748, and its thirty odd pages are delightful and thrilling to read since they are so full of common sense and so free from 'hypothetical reasonings' which, he says, so frequently misled physicians in the past. Cadogan was scathing, too, about the midwives of his day for on page 4 he wrote '. . . there is great reason to fear that those Nurses, who yet retain many of these traditional Prejudices (the use of herbs, roots and drugs etc.) are capitally mistaken in the Management of Children . . . and often do much harm where they intend to do good, by fancying Nature has left a great deal to their Skill and Contrivance'. A criticism which is still unhappily applicable in some measure to doctors and nurses today.

Cadogan was primarily concerned with the feeding and clothing of children, whom he said were 'in general overcloathed and overfed, and fed and cloathed improperly'. It was still the common practice, as originally advocated by Soranus, to salt the newborn and then to bind the head and limbs very tightly to prevent the development of deformities, and at the same time to restrict almost all movement. It was largely due to Cadogan's influence that swaddling was finally discarded. He also preached against another custom of his day, namely, as soon as the child was born, 'to cram a Dab of Butter and Sugar down its throat, a little Oil, Panada, Caudle, or some such unwholesome Mess so that they set out wrong and the Child stands a fair chance of being made sick from the First Hour. It is the custom of some to give a little roast Pig to an Infant which it seems is to cure it of all the Mother's longings' (p. 14).

If mother's milk was unobtainable, a wet nurse was the next best thing and she should be middle aged (i.e. between 20 and 30, a sad commentary on the expectation of life in the eighteenth century), but Cadogan believed that the current practice of sending the infant to be suckled 'out of doors' was less humane than exposure in the Roman fashion. Hand feeding, however, was equally dangerous since only one in three survived it and 'the skill of a good Physician would be necessary to manage it rightly'. Cow's milk should not be boiled because this alters the taste, destroys the sweetness and makes it 'heavier', and artificial food generally was not simple enough:

> 'Their paps, panadas, gruel etc. are generally enriched with Sugar, Spice and sometimes a Drop of Wine; neither of which they ought ever to taste', but he allowed beer at the end of the first year. 'They should not be laid on their Backs to be fed, but held in a sitting posture, that swallowing may be easier to them, and that they may more readily discover when they have had enough. When they have come to be about Six months old, and their Appetite and Digestion grows strong, they may be fed three times a Day; which I think they ought never to exceed their whole Lives after.'

Before concluding his brilliant essay Cadogan recommended early weight bearing to develop the limbs and plain speaking to the child rather than the use of the 'Mamby Pamby Stile'.

In submitting his work to the Governors of the Hospital, he asked them to regard it as a foundling 'to do with it what you will', and he concluded with this apt testimony to his own method: 'I am a Father, and have already practised it with the most desirable Success.'

N. Brouzet's essay on the 'Medicinal Education of Children and the Treatment of their Diseases' was published in Paris in 1754, and in London in the following year. It is well worth a close study for on page XIV of the Preface he shows at once that, like Cadogan, he has largely freed himself from the shackles of tradition:

> 'We have scarcely a single precept on the diet of children well established by a discussion of the advantages and inconveniences of the received practice. All that has been written on the choice of nurses and the nourishment of children is hardly anything more than a collection of prejudices.'

He dealt harshly with the sentiments of many previous authors and described Walter Harris's treatise as 'very short, and executed with little care'. Of normal breast feeding he wrote (p. 110):

> 'All nurses, and even those of Princes, that are under the direction of Physicians, give the breast to the infant as often as he seems to desire it, and wait until he leaves it himself. Thus the quantity is varied according to the appetite of the infants, and I believe there can be no danger in suffering them to satisfy their hunger.'

Indeed Brouzet is the first writer to take pity on the hungry baby who has been so sadly neglected in comparison with the overfed infant. His quotation from Joubert (Erreurs Populaires Tome I, p. 548) on page 61 bears repetition:

> '. . . our women are afraid of being slaves to their children; . . . but some of them are such slaves to their pleasures, that they won't suffer the wench to bring them the squalling brat to receive the breast if it is not his hour, but had rather that she would walk about with him, sing him some fine songs, or rock him till he goes to sleep . . . the infant whose belly is empty, and tormented with hunger before his usual hour, cannot sleep, and to appease or falsify him with a song is mere mockery. I would fain know whether the nurse, having a good appetite, would, instead of her supper, be contented with a song . . . We have a proverb which says "the hungry belly has no ears" and another "the empty belly is not easily contented with words". But I am in company says the lady, and would you have them bring my child, for me to shew my breast?'

Brouzet thought that ideally two, or at most three feeds daily would be the best method of promoting a healthy digestion, but he was sufficiently practical to appreciate that, whether one liked it or not, hungry babies must be fed more often.

He particularly displayed his originality with regard to breast milk for, so far as I am aware, he is the only historical writer on the subject, apart from van Helmont whom he quoted, to dare to suggest that it may not be the most suitable food for infants regardless of whether it comes from the mother or a wet nurse. Should we not try to improve upon nature and provide an aliment which is free from the defects of breast milk? He proceeded to discuss the problem by asking three questions (p. 76):

(1) Should infants be nourished with milk? Universal approval satisfied him that they should, but van Helmont had advised feeding with panada made of bread slightly boiled with small beer, sweetened with clarified honey and finally diluted with beer to make it fluid, a mixture which would not become sour or corrupt, and which was free from the diseases and vices transmitted by milk. Brouzet pleaded for large scale experimentation to test the efficacy of van Helmont's formula for, as he wisely commented, 'reasoning alone can never be the foundation of medicinal precepts'.

(2) Should infants be nourished with woman's milk? 'All the people in the north feed their infants with cow's milk and it is universally allowed that these people are stronger and less subject to diseases than the southern nations.' He concluded that there was no evidence against cow's milk and weaning difficulties at nine months are obviated by its use.

(3) Should it be the milk of their own mothers? In spite of the sentiments of moralists, male midwives, politicians, writers and many physicians, Brouzet pointed out that a wet nurse may be more healthy and her vices may differ in quality from those of her mother, but on the other hand they may be less serious than those commonly found in wealthy women. He pooh-poohed the popular notion of a close harmony between the baby and his mother's milk, and the idea that an infant may thrive on a smaller quantity of it was, to his practical mind, absurd, though he believed that it was important for the stage of lactation in the nurse to correspond with the age of the suckling.

Brouzet concluded, somewhat tentatively, that cow's milk, goat's milk or van Helmont's formula are perhaps best of all, but he recalled that he himself sucked a drunken nurse for about 18 months with conspicuous success.

Finally he tackled the thorny problem of the advisability of prohibiting sexual intercourse during the period of lactation, treating the subject with typically French frankness. After some speculation he arrived at the conclusion that it is better for the nurse to enjoy the company of her husband than burn with the passions of unsatisfied desire, and by way of adding a personal recommendation he confided that he had not avoided lying with his wife and making love to her at these times yet their children had been well suckled. This moderate attitude has been paralleled in recent years over the question of smoking and drinking during the lactational period.

George Armstrong (? 1712-1764) opened the first dispensary for children in Red Lion Square, Holborn, where Walter Harris had died, and where William Cadogan, Jonas Hanway and James Nelson the apothecary lived. He wrote an 'Account of the Diseases Most Incident to Children' which was published in 1767 (revised edition 1783) based upon the experience he had gained whilst working amongst the children of the poor, to which was added an 'Essay on Nursing', a subject which was still commonly left to old women, nurses and midwives.

Armstrong was not particularly interested in breast feeding though he made the engaging comment that fond and anxious mothers sometimes make bad nurses, and he advised that a good wet nurse should have strong nerves lest the least surprise affect the milk, or sickness of the infant cause it to dry up when it is most needed. Hand feeding concerned him more presumably because of his work amongst the poor, and his own two children were reared in this way. 'There are two ways of feeding by hand; the one is by means of a horn, the other is with a boat or a spoon. They both have their advocates; but the latter, in my humble opinion is preferable' (p. 157). We shall include his graphic description of the horn in the section on the evolution of the feeding bottle in Part IV.

If the infant was to be hand fed from birth it should be given 'new cow's milk mixed with its victuals as often as possible, and now and then some of it alone to drink. Asses milk will be still better when available and the parents can afford it.' If the cow's milk was not 'new' it should be boiled and the pap, with which it was mixed, should be made from rolls rather than loaves since the latter were commonly bleached with alum. Hitherto most writers had regarded sugar merely as a flavouring agent, but Brouzet and Armstrong were among the first to appreciate the nutritive value of Lisbon sugar, though his recommendations in an earlier edition that it should be added to milk was not altogether well received (see his footnote to p. 161):

> 'A very ignorant writer in the *Political Register* observes upon this passage, that there should be no sugar at all put into children's food; and the reason he gives for it, lest it should ferment in their stomachs. If this sage doctor was as skilled in his profession as one who sets up for a critic in it ought to be, he would certainly have known that digestion is partly a fermentatory process.'

At the age of 5 or 6 months the feeds should be thickened and broth, beef tea, minced chicken and bread pudding should be added gradually, with a rusk for the infant to chew as early as possible.

Armstrong described pyloric stenosis, but according to Still (1931) the first description emanated from Patrick Blair in 1717.

Hugh Smith (1730-90), Physician to the Middlesex Hospital, wrote several 'Letters to Married Women on the Nursing and Management of Children' which were published together in 1792 in a volume which might be described as the prototype of the modern mothercraft manual. In it, as might be expected, he strongly recommends breast feeding and indeed he apologizes for the necessity of having to raise such an obvious point at all. He believed that colostrum should be given to the newborn, that frequent suckling stimulated lactation, and that four hourly feeding at 7 a.m., 10 a.m., 1 p.m., 6 p.m. and 11 p.m. approximately is satisfactory after the first month. For hand feeding Smith advised the use of cow's milk (the 'properest substitute' for breast milk), which should be boiled if it purges, sweetened with Lisbon sugar if it constipates and be partially skimmed if it is a rich country product.

In Letter IX on page 124 he wrote in his amusingly intimate style:

> 'What we have next to observe is the quantity of milk proper to a newborn child in 24 hours. What think you, my dear ladies, of a Winchester pint being a sufficient quantity for the day and night? Methinks I hear an exclamation—O barbarous man! Under a pretence of correcting us he intends to starve the little helpless creatures! Was there ever such a cruelty heard of before? Allow a child only a pint of milk a day! Why it would eat two quarts of pap and still cry for more——. Yet after all surprise an infant in the month will receive from one pint of milk more real and good nourishment than from ten quarts of pap . . .'

On a subsequent page Smith set down the actual quantities of undiluted cow's milk to be given to infants of various ages (calculation of a feed on the basis of the weight did not begin for another 100 years), and he was the first author to do so. During the first month 1 pint daily was to be given equally divided into four feeds, and this was gradually to be increased to 2 pints daily in five feeds by the age of 3 months, and thence up to 3 pints if the infant is still hungry but 'in whatever way you manage children, be careful not to feed them overmuch'.

Hugh Smith is an important figure because we find in his writings the above views on the time and size of feeds, a description of his famous invention the 'bubby-pot' (to be included later), and the earliest signs of an awakening interest in, and awareness of, the constituent properties of milk, for he advised the addition of broth if the animal element was lacking and he pointed out that breast milk is deficient in cream and curd, whereas asses' and mare's milk approached nearest to human milk in constitution, yet cow's milk is cheapest and therefore best.

William Moss (? -1802), a Liverpool surgeon, is the last eighteenth century writer to merit individual attention since his 'Essay on the Management, Nursing and Diseases of Children', published in 1794, contains a large section on infant feeding which is full of good sense. Moss regarded breast milk as a perfect blend of animal and vegetable matter, or as a 'semi-digested intermediate state between the two', and he believed that the gastric juices of each animal were specially suited to the milk of that species. He was the first writer to challenge the traditional belief in the purgative action of colostrum, based upon his own observations made in the true scientific spirit that older babies, when put to the breast of a newly delivered woman to draw out her nipples, were not purged and that neonates, when fed with established milk from birth, did not require purgation in order to rid themselves of meconium. The use of colostrum was to him both natural and proper, especially since the common practice of giving pap and panada in the first week of life often lead to gripes, and even death, before the breast milk came in.

In appreciating, as Hugh Smith had done, the similarity between human and asses' milk Moss was clearly influenced by the analyses of Thomas Young whose work first appeared in the form of a learned M.D. thesis entitled 'De Lacte' at Leyden in 1761.

Moss believed that infant nursing was a subject of vital importance and for this reason his relationship with nurses and midwives was not a happy one for he deplored their habit of chewing the food first, and he deprecated the fact that many appeared to have complete dominion over the child, that they seldom submitted to medical advice and direction, that they were bound by prejudice and tradition and that they resented all interference as implied adverse criticism. Incidentally, one of the midwives' duties was to sever the lingual frenum with her finger nail, an operation which was as frequently, and as

unnecessarily, carried out as circumcision is today. He considered that one baby in every three or four had tongue-tie and that this was one of the commonest causes of breast feeding difficulties.

The latter half of the eighteenth century, as we have seen, witnessed a remarkable awakening of interest in the welfare of infants which, taken in conjunction with improved methods and deeper knowledge of infant feeding, was rapidly rewarded by a steady and profound fall in the appallingly high death rate of infants and children under the age of 5.

FIG. 7.—Feeding infants directly with asses' milk at the *Hospice des Enfants Malades*. Reproduced from Sadler's 'Infant Feeding by Artificial Means' by kind permission of Messrs. Routledge and Kegan Paul.

At the close of the century four principal methods of infant feeding were extant:

(1) Breast Feeding by the Mother. This was usually practised with the early addition of pap. Only van Helmont and Brouzet were dubious of the supremacy of breast milk but their views were not widely held, even in France where an earlier writer, Jean Astruc (1746), had paid a fine tribute in a lecture in Paris to the far-reaching value of breast feeding:

> 'Nor should children be weaned until they are eighteen months or two years old, for the longer they suck the better, as good breast milk not only prevents many ailments, softens and cools the gums when inflamed, forwards dentition, and prevents its fatal consequences, but even lays a lasting foundation for a robust and healthy constitution and would prevent our having a diminutive generation of which our age is too productive.'

(2) Breast Feeding by Wet Nurses. The limitations of these women who 'were mainly destitute of all reason, knowledge and principle: in short of almost everything except mercenary prospects' did not prevent William Buchan (1779) from recognizing the value of breast milk from whatever source it came:

> 'Nature not only points out the food proper for infants, but actually prepares it. This however is not sufficient to prevent some who think themselves wiser than nature from trying to bring up their children without her provision. The mother's milk, or that of a healthy nurse, is unquestionably the best food for an infant. Neither art nor nature can provide a proper substitute for it.'

The transmission of character and temperament by breast milk was widely believed in, but for some reason the intellect of the growing infant was not liable to be affected in the same way; hence the increasing popularity of asses' milk

(3) The Use of Animal Milks. The latter half of the century saw an increasing interest in the use of animal milks in infant feeding though they had of course been widely used before, mainly by the peasant class. In Paris J. C. Desessartz (1760) recommended human, ass, goat, cow or ewe's milk in that order of preference based upon the size of the curd, and in the following year Young's thesis was published at Leyden. Alphonse Le Roy (quoted by Drake, 1930) was a great believer in the vital principle of milk, and in 1775 he instituted at Aix the direct suckling of foundlings by goats:

> 'Each goat which comes to feed enters bleating [into the ward] and goes to hunt the infant which has been given to it, pushes back the covering with its horns and straddles the crib to give suck to the infant. There is in milk, beside the different nutritious principles, an invisible element, the element of life itself, a fugitive gas which is so volatile that it escapes as soon as the milk is in contact with the air. This is why it is impossible to rear infants with animal milk or with milk which has been expressed from the breast.'

(4) Pap and Panada. Almost all the medical writers of the eighteenth century were appreciative of the danger of this mode of feeding, particularly when pushed to excess, but even as late as 1813 James Hamilton of Edinburgh (quoted by Drake, 1931) wrote that 'pap and panada be now almost universally used for the first food of infants, as a substitute for the mother's milk'.

In the nineteenth century we shall observe a

decline in breast feeding as a result of the employment of women during the Industrial Revolution and a gradual falling off in the popularity of wet nurses except on the Continent, together with the supersession of various artificial foods as a substitute for breast milk, based upon primitive scientific principles. Pap and panada survived only amongst the most backward sects of the community, and the direct suckling from animals became prevalent only in France.

Nineteenth Century Writers

Michael Underwood's 'Treatise on Diseases of Children' in three volumes was first published in 1789. The fourth edition (1799) was the first to include, on the fly-leaf, a detailed chemical analysis of milk—a very important milestone along the road to the scientific approach to infant nutrition, the road which began with the famous nail test. The seventh edition (1819) bears the first real resemblance to a modern paediatric textbook and the third volume is entirely devoted to the management of infants including infant feeding.

The first fifty odd pages are filled with Underwood's views on Dr. Clarke's findings on the composition of human milk in Dublin in 1786, and the discourse which, beneath the veil of courtesy, has a distinctly acrimonious tone, is interesting to follow. According to Underwood, Clarke had asserted that: 'Woman's milk in a healthy state contains no coagulable or cheesy principle.' Underwood found by experiment that this was not so, but he noted that the curd took longer to form and was smaller which, he felt, reflected its added suitability for infants.

'If we find human milk out of the body so very slow in running into an acescent state, does it not afford strong presumptive evidence that the milk of nurses cannot be so very prone to run into acidity in the stomach of infants as authors endeavour to persuade us?' This assertion of Clarke's challenged the teaching of Walter Harris and was therefore repugnant to Underwood, though it must not be concluded that he completely accepted Harris' teaching, for on page 160 he relegated the role of acidity to a secondary place in the aetiology of infant disorders, 'the natural acid becoming morbidly acrid through overfeeding and other errors in the diet', and this acidity then aggravated the general condition. Underwood confirmed that breast milk was slow to turn sour *in vitro* though the rate varied with different samples; he kept specimens of human and cow's milk for long periods in phials on his mantelpiece, observing from time to time the development of the sour and putrid taste and smell. He concluded from these experiments that the souring process was fundamentally the same in both milks and that acidity was a cause of infantile dyspepsia, for did not breast fed pukings contain cheesy curds and turn litmus red?

Dr. Clarke had asserted that green stools were not a sign of acidity since *in vitro* most acids do not turn bile green. This argument carried no weight at all with Underwood for if some acids did then that was sufficient for him, and in any case infants who vomited frequently passed loose green stools which smelt sour and turned litmus red also.

With such crushing arguments at his disposal it is perhaps a little difficult to see why it was necessary to devote over fifty pages of the Introduction to them.

On the question of breast feeding, Underwood noted that it was becoming increasingly fashionable for ladies of rank to be maternally minded so that the evils of wet nurses and baby farming were declining and attention to difficulties at the breast was growing. In fact he seems to have been the first writer to have considered why it was that animals had so little trouble compared with man, and he concluded that the reason was that the latter had been 'designed to be the pupil of observation' with 'scarce any innate discernment'. In addition to these philosophical problems, he was also concerned with the mechanical barriers to successful lactation; thus on page 79 he recommended the use of Mrs. Relf's nipple shield for tender or retracted nipples which could be obtained from Mr. Savigny, surgeon's instrument maker, of Covent Garden. Underwood's interest in breast feeding, which might be likened to an oasis in the surrounding desert, has therefore many similarities to the work of Dr. Waller over 100 years later.

With regard to artificial feeding he closely followed the teaching of Hugh Smith whose bubby-pot met with his approval because the infant was made to work for his food rather than be overfed before he realized it; 'fed by means of it they are often hungry, and that is its highest recommendation.' Nevertheless he believed that in London only about one in eight survived hand feeding, and that those who thrived on spoon feeding would probably survive any regime, but 'art and good management may save many infant lives'.

Thomas Bull wrote the 'Maternal Management of Children' (3rd edition 1848) and 'Hints to Mothers' (1849), and set down the following rules for nursing for the guidance of mothers whose duty it was to breast feed their own children: (1) Put the newborn infant to the breast a few hours after delivery to draw out the nipples and stimulate secretion. The

dosing of the newborn with castor oil or honey of roses and almond oil, though a common practice among midwives, was quite unnecessary. Of colostrum he wrote:

> 'It has been supposed by some that the milk first secreted is improper for the child—that it teases the bowels. The fact is, that it differs in an important respect from that which is secreted soon after; but then it is a difference which nature has ordained and designed for a wise purpose.'

Bull felt that primiparae would seldom be able to satisfy their offspring during the first four days of life, and for this period he advised offering half-strength asses' milk or one-third strength sweetened cow's milk from a sucking bottle.

(2) The frequency of feeding must depend upon the infant's appetite during the first ten days.

(3) For the rest of the first month regular four-hourly feeds day and night were advised. Irregular feeding resulted in overloading of the stomach, dyspepsia, fever and often death.

(4) After the lying-in period an effort should be made to eliminate the night feed and so rest the mother. If possible, breast feeding without additions should continue until the teeth erupted; he deplored the still prevalent practice of giving panada, gruel or Naples biscuit during the first six months. Half-strength cow's milk was the substitute for the breast that he relied upon.

(5) Soon after the teeth appear, diluted cow's milk, farinaceous foods, broth, beef tea, etc. should be gradually introduced so that weaning was completed by the age of 12 or 18 months.

Bull mentioned that green stools, irritability and posseting were liable to occur in the breast fed baby when the mother was menstruating which necessitated temporary removal from the breast for young babies or complete weaning for older ones, as would a fresh pregnancy for infants of all ages. Wet nurses were considered to be preferable to hand feeding, and the usual characteristics are to be found indicating that even in the middle of the nineteenth century there was a lingering belief in the transmission of the passions in the milk. Before engagement the nurse should be asked whether menstruation had returned and in this respect there was no fear of concealment for it was commonly held that menstruation rejuvenated the milk though Bull recommended that if this was the case she should be rejected.

He was the first author to devote due consideration to the importance of psychological factors. He gave a very full account of a nervous mother's lack of experience in nursing and as this is the first detailed case history to be found in the literature it is worth recording in précis form.

> A young mother gave birth to a healthy first baby whom she fed satisfactorily for three weeks. Then, in spite of an abundance of milk, the motions became lumpy, of mixed colour and dry, they were passed with great pain and frequent fits of crying occurred. The infant soon began to lose weight, the screaming fits became more frequent and violent especially after feeds until he fell back exhausted to sleep. 'It was very evident that the infant's hunger was not satisfied or its body nourished by the parent's milk, which, although abundant in quantity (the breast being large and full of milk), was at this time seriously deteriorated in quality. This was caused, I believe, from great anxiety of mind. Her monthly nurse became suddenly deranged and the whole responsibility and care of the child thus devolved upon the mother, while she was entirely ignorant of her duties. A wet nurse was obtained. In a very few hours after this change was effected, the screaming ceased, the child had quiet and refreshing sleep, and in twelve hours a healthy motion was passed.' He thereafter grew up into a fine healthy boy and the mother subsequently proved herself to be a good nurse to two later children.

It is entertaining to speculate upon the correct diagnosis here for we need not accept his conclusions without reservation, but we may certainly applaud his initiative in setting the facts before us. A more difficult problem to solve is to be found in von Ammon's remarkable story, which Bull repeats, of a nursing mother who separated her husband and another man who were fighting and then picked up and suckled her baby at once; he immediately died in her arms.

Charles West (1816-98), co-founder of the first children's hospital in the British Isles in Great Ormond Street in 1852, delivered a series of lectures on paediatrics to the students of Middlesex Hospital which were first published in 1848. Lecture 27 in the first edition, and Lecture 31 in the revised seventh edition of 1884, were solely concerned with infant feeding. It is of interest to compare and contrast the two lectures and thereby gain some insight into the progress made during the 36 years that intervened.

West put considerable emphasis on the chemical analyses of human and animal milks, quoting Professor Simon's 1838 figures in the first edition and Vernois and Becquerel's 1853 results in the later one. There was marked disagreement between the two sets of analyses but it can hardly be said that the French figures were notably more accurate than the earlier Berlin ones for both of them made the casein content of human milk extremely high, namely 3·1 and 3·9% respectively. Nevertheless they were sufficiently accurate for West to deduce that asses' milk was a suitable substitute for breast milk and that cow's milk required diluting and sweetening to become 'humanised'. The micro-

scopical examination of milk was coming into importance and the reaction was also studied. Breast milk and milk from cows at pasture were alkaline to litmus whereas a stall-fed cow produced milk which required diluting with lime water.

Even in the later edition there is a paragraph on the choice of a wet nurse who, in addition to the usually recommended features, should be a robust brunette. The partiality was presumably inspired by the work of L'Heritier who had analysed the milk of one blonde and one brunette and had found the latter's more nutritious. It was perhaps fortunate for blondes and redheads that wet nurses were dying out.

Two other points of interest appear for the first time in the revised edition. First, condensed milk gets its first mention though West was not very enthusiastic about it, pointing out that it contained less fat and albumen and more sugar than fresh milk so that it was less nutritious and more dyspeptic. Secondly, the test feed, though not described by that name, gets its first mention in an English textbook having first been described by M. Guillot in 1852 who, working at the foundling hospital in Paris, observed that infants under 1 month old, when weighed before and after feeds, recorded an increase of from 2 to 5 ounces, from which he calculated that they required about 1,000 g. daily, i.e. 10 3-ounce feeds approximately. West was clearly markedly influenced by the work of contemporary Frenchmen, but he did not accept M. Tarnier's rejection of the feeding bottle on hygienic grounds, for he likened the alternative method of spoon feeding to the manner of fattening turkeys—there was no option but to take it or choke!

Pierre Budin (1846-1907), the famous French obstetrician and pupil of Tarnier, is the last important, but by no means the least important, nineteenth century writer on infant feeding. His published lectures were delivered in Paris at the end of the century though they were not translated into English by W. J. Maloney (under the title of 'The Nursling') until 1907. As a result of Budin's work, French influence upon English paediatrics, which was prominent during the latter half of the nineteenth century, was carried over for several years into the twentieth.

Budin was a firm advocate of breast feeding and at the *Maternité* he maintained a permanent staff of wet nurses to suckle weaklings and other infants who would otherwise be deprived of breast milk. Furthermore he was proud to be able to state that 60% of the babies attending his clinic were wholly breast fed and 34% were partially breast fed, though these figures were not flattering since there must have been a strong tendency for the bottle-fed babies to continue to attend whereas the others would require less supervision.

If, however, breast milk was not available he prepared sterilized undiluted cow's milk which was distributed daily in sealed bottles each containing the appropriate quantity for one feed. This was notably unorthodox:

> 'When I first advocated the feeding of infants on undiluted milk, critics asserted that infants could neither support nor digest it, and that it was responsible for quite a catalogue of evils—digestive troubles, rickets, eczema, urticaria, etc. I have never seen any bad trouble from its use.'

Cow's milk, because of natural variation and illegal dilution with water, was not of constant composition so he took care to ensure that the milk he distributed contained approximately 37·35 g. per litre of butter fat. His insistence on sterilization was inspired, as he freely acknowledged, by the work of Pasteur, and he did not subscribe to the common view that heat treatment destroyed certain vital principles in the milk, for he asserted that no case of rickets or scurvy developed under his care and he believed that these diseases were caused by over-dilution.

At his *consultation de nourissons*, the first of its kind in the world, accurate weight charts of each attending baby were kept, very similar to those in common use today. He accepted Bouchaud's figures for the average weight gain for a normal infant, namely 1 oz. daily for the first two months of life, $\frac{5}{6}$ oz. for the second two months and $\frac{2}{3}$ oz. for the third two months. He seems to have arrived at the correct food requirements by a process of trial and error; his formula was calculated by multiplying the infant's weight in grammes by two, and discarding the last digit. This gives a daily intake equivalent to $\frac{1}{5}$ body weight (the modern estimate of $2\frac{1}{2}$ oz. per lb. is rather less than $\frac{1}{6}$ body weight), and he appreciated that infants weighing less than 2·8 kg. required proportionately more. In common with all the previous writers, he described overfeeding as the 'scourge of infancy' and stated that 'it was better at first to give too little than too much' for an underfed infant failed to gain weight but it was free from digestive troubles. He mentioned one infant who showed a normal weight curve on an intake of only $\frac{1}{10}$ the body weight daily and curiously enough this has been taken to be his standard recommendation (see Powers, 1935, 'Budin's Rule'). Budin repeatedly reiterated his views on the danger of overfeeding.

In summary it may fairly be stated that Budin clearly and intelligently laid the firm foundations for

the modern practice of infant feeding based upon breast feeding wherever possible or the use of sterile milk in quantities calculated according to weight rather than age which had hitherto been customary. His repeated insistence on the danger of overfeeding is readily understandable against the sombre background of epidemic cholera infantum prevailing at the time, but it was unfortunate that his followers saw fit to exaggerate his teaching and thus condemn a large number of French babies to a regime of chronic underfeeding.

Other Nineteenth Century Works. It would be tedious and unnecessarily repetitive to describe in detail the writings of all the nineteenth century paediatricians, but a few brief comments on the remainder will now be made.

C. A. Struve was a German physician whose work 'A Familiar Treatise on the Physical Education of Children' was translated into English by Willich in 1800. As Still (1931) has commented, it is difficult to see how the contemporary English could have derived benefit from this work which was definitely less advanced than those of Hugh Smith, Moss and Underwood.

C. H. F. Routh wrote an interesting book entitled 'Infant Feeding and Its Influence on Life' second edition 1863, in which he showed that he was fully aware of the effect of diet upon infant morbidity and mortality, and he was one of the earliest writers to marshal statistics to prove his point.

Eustace Smith produced a work on 'The Wasting Disease of Infants and Children' which contained a large section on infant feeding in which he advised the practitioner to give 'plain, minute and exhaustive' instructions on the recommended diet for an infant; his own directions admirably followed the pattern he had set.

Other late nineteenth century writers included Angel Money (1887), Mrs. Sadler (1896), who compiled facts and fancies from the works of contemporary experts, A. A. Beale (1894), whose comprehensive booklet on infant feeding and management cost only one shilling, and the appropriately named Pye Chavasse (1852) whose 'Counsel to a Mother' is both pompous and pontifical. Many paediatric textbooks were being born at this time such as those of J. F. Goodhart of Guy's, Ashby and Wright of Manchester and Emmett Holt of America, and all of them contained one or more chapters on infant feeding which summarized the current views of the day.

W. B. Cheadle's lectures on artificial feeding, six in all, were delivered at St. Mary's Hospital, London, and also at Great Ormond Street in 1887 (published in 1892) and are full of interest, especially with regard to his original views upon fat deficiency and rickets, lack of fresh foods and scurvy, and the use of raw meat juice and bread jelly.

Finally, Edmund Cautley (1897) produced by far the most complete and comprehensive textbook on infant feeding for the use of students and practitioners. It was over 400 pages long, comprising sections on the physiology of lactation, the management of breast feeding, the character and composition of breast milk with the factors liable to cause alterations in it, contraindications to breast feeding, weaning, comparison of cow's milk and breast milk, artificial feeding and the modification of cow's milk, proprietary infant foods, Dr. Vaughan's 'tyrotoxican' and micro-organisms in milk with its heat treatment, the feeding of prematures and the growth of normal infants. In fact this is the prototype of the modern textbook on infant feeding.

BOOK REVIEWS

The Normal Child: Some Problems of the First Three Years and Their Treatment. By R. S. ILLINGWORTH. (Pp. 342; 63 drawings. 30*s*.) London: J. and A. Churchill. 1953.

Having unwrapped the parcel, the reviewer must admit to a groan as he contemplated what he thought was just another book on the 'welfare' infant. His fears were unfounded. It is true that there is a good deal of material on growth and development, infant feeding, vitamins, and so on, but they are all treated much more thoughtfully and with less evangelism than usual. The advantages of breast feeding are an article of faith with British paediatricians, and Professor Illingworth displays this well but with reason and humanity in place of bigotry, and finds space to include the few disadvantages. He is exceptionally well read, and one suspects occasionally that a reference has been included for completeness, because there is a card in an index, but in general this inclusive tendency leads only to a fair discussion of all major aspects of a subject. Some authors leave the reader to work out his own conclusions, but Professor Illingworth finally sums up his reading, modified by his experience, and tells you what he thinks.

Recent textbooks deal well with clear-cut diseases, but much of paediatrics is concerned with disturbances of behaviour and development. Psychiatry can claim some successes in the grosser abnormalities, but in considering minor disorders which are important to parents (such as insomnia or masturbation), one is accustomed to ignore the new volumes with their intact dust covers and go straight to the well-thumbed Still. Many paediatricians will probably now first pick up Illingworth's slim volume, flipping the pages over as they scan their page headings: accident prevention, keeping the child busy, toys and play, shyness, thumb sucking, breath-holding attacks, refusal of food, effect of hospital, discipline, favouritism, etc. This book fills a need.

Growth of Children. Sixty-six Boys and Sixty Girls Each Measured at Three days and at One, Two, Three, Four and Five Years of Age. By ALEXANDER LOW. (Pp. 63. 10*s*.) Aberdeen: University Press. 1952.

For a considerable time rumours of a longitudinal growth study of children in Aberdeen have been periodically reaching the fastnesses of the South. Now, at last, come the documents; and they make up for the lateness of their appearance by their unsurpassed completeness. This book consists of the actual raw measurements of 66 boys and 60 girls taken at 3 days old, 1, 2, 3, 4 and 5 years. The measurements were all made by the late Professor Alexander Low, and the publication appears over the hands of Miss A. M. Clark, Mr. M. H. Quenonille and Professor R. D. Lockhart. We are most indebted to them, measurer and publishers alike, for, although one can never be sure of this sort of data without a little mathematical analysis, on the face of it these appear to be the best records of bodily growth from birth to 5 years yet published anywhere. Eight measurements of the head and face, and 13 of the body, are given; and there are no gaps in the data. A minor criticism is that stature and sitting height were taken with the child lying down from birth to 3 years (crown-heel and crown-rump lengths) but erect from 3 to 5. The result is that the increment from 3 to 4 is too low, the lying values for these measurements always being the larger. This throws into relief one of the many difficulties of longitudinal studies, that of maintaining constancy of methods over long periods of time, or providing duplication over an adequate period if advances in technique simply cannot be denied.

Information on age of parents, pregnancy number, date of cutting first tooth, bottle or breast feeding, number of teeth at 1, 2 and 3 years and size of fontanelle is also given. The children were born between 1923 and 1927, so the records give us a picture of growth rate during the decade 1923-32. Unfortunately the social and economic background of the homes is not mentioned. Enthusiasts of the biometry of growth will find much in this data to extract, and it is to be hoped they will sharpen their calculators carefully, for Professor Low's patient, unspectacular and persistent labours deserve well of them.

Human Milk. By S. D. MORRISON. (Pp. 91; illustrated. 10*s*. 6*d*.) Farnham Royal, Bucks: Commonwealth Agricultural Bureaux. 1952.

This is a valuable collation of the published data on the yield and the protein, fat, sugar and minerals of human milk. It is made from the point of view of a laboratory milk chemist, and as no dairy industry has been founded with women as chief producers, most of this interesting information is not of immediate practical usefulness to clinicians.

The variations in milk composition between different healthy women and from time to time in individual women are well brought out. In practice we deal with a nursing couple and we assume, probably rightly, that the composition of the milk produced by the mother, although variable, is suitable for the infant and hence what matters is the volume. The various reports on milk yield are not well digested here, chiefly because it is not made clear that figures from test weighings are not comparable with figures from expression of milk by hand or by pump. The failure to notice Waller's work (e.g. *Nursing Mirror*, Jan. 15 and 22, Feb. 12 and 19, 1949;

Lancet, 1950, **1**, 53) on residual milk obtainable by expression after the infant has fed, is extraordinary.

Waller's figures (*Arch. Dis. Childh.*, **21**, 1) for daily amounts of milk secreted on each of the first 13 days after delivery by two groups of 100 primiparae and a third group of 100 multiparae are not noted although certain daily volumes estimated by multiplying one milking by five are given. In Waller's work the babies of the multiparae took on an average 9 oz. of milk on the fourth day. A mean figure of 32 oz. obtained (by expression) from seven women on the fourth day is quoted with details of each woman's yield. This might have received more discussion for, if the babies average 7 lb., this is 4½ oz. per lb. body weight on the fourth day of life. Yet on page 9, in dealing with Roderuck's findings on variation in volume of milk at different stages of lactation, the author suggests that manual expression tends to reduce milk flow in the lying-in period. Surely the explanation of the observation that the daily milk yield by expression, on five successive days at 70, 160 and 300 days of lactation, increased from the beginning to the end of the test period is that the increased demand (or better emptying) led to rapid increase of output. This explanation would have sprung to the author's mind if he had studied Budin (Budin, P.C., 1907, 'The Nursling'). Is it worth seeing 'a general tendency' in the yields obtained for three primiparae compared with three multiparae and is it 'safe to assume' that all the subjects in a home for unmarried mothers are primiparae? Some girls never learn.

There are many questions on which the author might have collected and criticized available information. Our practice in this field of medicine is largely by rule of thumb but there may be more information available than we know. For example, much public money is spent on cotton seed oil as a galactagogue. The author has collected evidence that increasing fluid intake does not increase milk output. Is this true about other reputed agents? Are prolactin preparations efficacious?

It may well be that the author has thought of the problem only from the dairy chemist's point of view, but the field worker is interested also in the efficiency of breast feeding by various nursing couples. Is the incidence of successful breast feeding for say, six months, correlated with the yield in the early days of lactation? Is the quality of good lactation transmitted by the male as in the bovine species?

Though it is not comprehensive, this is a useful book, well made and reasonably priced. We still need a book combining chemical knowledge with results known from dairy research and clinical observations on breast feeding in the human species.

Fibrocystic Disease of the Pancreas. Edited by M. BODIAN. (Pp. 244; 133 illustrations. 63*s*.) London: Wm. Heinemann. 1953.

In this monograph a clinician, a geneticist and a morbid anatomist join forces to describe and analyse a series of 116 cases of fibrocystic disease of the pancreas seen at The Hospital for Sick Children, Great Ormond Street. They conclude that, far from being simply a pancreatic lesion, this is a pluriglandular disease genetically determined and characterized by the secretion of abnormal mucus. On this conception it is unlikely to be curable, but general supportive and anti-infective treatment has led to a much better survival rate than was seen a decade ago.

The biggest section of the book is devoted to a study of the morbid histology of the disease, and a wealth of tables and photomicrographs of an outstanding order illustrate and clarify the points made by the authors in a fashion that even the rustiest histologist cannot fail to appreciate. There are tables of biochemical findings and short summaries of all the cases, and the book ends with a short chapter on other pancreatic dysplasias.

It is desirable that from time to time apparently new or at least unrecognized conditions should be the subject of an authoritative description and discussion, and a warm welcome will be assured in paediatric circles for the present volume.

Les Vomissements du Nourrisson. By EMILIO ROVIRALTA. (Pp. 209 plus bibliography; 80 illustrations. Fr. Frs. 1,800.) Paris: Editions Médicales Flammarion. 1952.

This is not—nor is it meant to be—a comprehensive and authoritative treatise on the subject of vomiting in babies. The author sets out to question certain generally accepted and often empirical views on the subject and to advocate more detailed clinical analysis and more frequent use of radiological investigation. Largely as a result of adopting such principles it has become possible of recent years to separate from the heterogeneous group of babies with vomiting of uncertain origin—often classified as habitual vomiting—certain clearly defined syndromes. Many of these are the result of specific anatomical defects. Commensurate with a better understanding of the underlying pathology a more rational and effective treatment has become possible. One such example is afforded by the partial thoracic stomach. This condition is well reviewed, although the method illustrated for propping up an infant seems, at first sight, to carry a possible risk of strangulation! By contrast, however, other affections, notably diaphragmatic herniae and intestinal obstructions, are discussed extremely sketchily and there would appear to be little merit for their inclusion in this book. Other subjects considered include pylorospasm, certain aspects relating to the aetiology and treatment of pyloric stenosis, duodenal obstruction and vomiting occasioned by the compression and displacement of the stomach secondary to a distended, gas-filled transverse colon. Many views expressed on treatment and aetiology are controversial but serve possibly to stimulate discussion. Radiographic illustrations are of variable quality.

Although there is an extensive bibliography its value is considerably reduced by the failure to include many references made in the text. These too are often inaccurate and the spelling of authors' names frequently variable and incorrect.